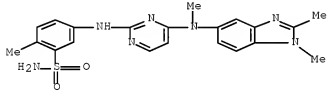
***** QUERY RESULTS *****
(ELECTED SPECIES # 1)

⇨ d ide l3

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 868945-46-4 REGISTRY
ED Entered STN: 30 Nov 2005
CN Benzenesulfonamide, 5-[[4-[(1,2-dimethyl-1H-benzimidazol-5-yl)methylamino]-2-pyrimidinyl]amino]-2-methyl- (CA INDEX NAME)
MF C21 H23 N7 O2 S
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

⇨ file stng
FILE 'STNGUIDE' ENTERED AT 10:48:17 ON 28 JAN 2008
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT © 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 25, 2008 (20080125/UP).

=> d his l6

L6 1 S L3

=> d que l6
L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON "BENZENESULFONAMIDE, 5-((4-((1,2-DIMETHYL-1H-BENZIMIDAZOL-5-YL)METHYLAMINO)-2-PYRIMIDINYL)AMINO)-2-METHYL-"/CN
L6 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

⇨ d l6 ibib ab

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1196402 HCAPLUS Full-text
DOCUMENT NUMBER: 143:452849
TITLE: Pyrimidine derivatives and quinazoline derivatives for

cancer treatment
INVENTOR(S): Mullin, Robert John; Gilmer, Tona M.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Kumar, Rakesh
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105094	A2	20051110	WO 2005-US12337	20050412
WO 2005105094	A3	20060615		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1755394	A2	20070228	EP 2005-735666	20050412
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV				
JP 2007532658	T	20071115	JP 2007-508465	20050412
US 2007208023	A1	20070906	US 2006-599967	20061016

PRIORITY APPLN. INFO.:
US 2004-563285P P 20040416
US 2004-605288P P 20040827
WO 2005-US12337 W 20050412

OTHER SOURCE(S): MARPAT 143:452849

AB A method for treating cancer is described including administration of a pyrimidine derivative and a quinazoline derivative Also described is a pharmaceutical composition including the same. Compound preparation is included.

***** QUERY RESULTS *****
(ELECTED SPECIES # 2)

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=> d l5 ide

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2008 ACS on STN
RN   231277-92-2  REGISTRY
ED   Entered STN:  07 Aug 1999
CN   4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-
     [5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-  (CA INDEX
     NAME)
OTHER NAMES:
CN   4-[[3-Chloro-4-(3-fluorobenzyloxy)phenyl]amino]-6-[5-[[(2-
     methanesulfonylethyl)amino]methyl]furan-2-yl]quinazoline
CN   GSK 572016
CN   GW 572016
CN   Lapatinib
CN   N-[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]-6-[5-[[[2-
     (methylsulfonyl)ethyl]amino]methyl]-2-furyl]-4-quinazolinamine
MF   C29 H26 Cl F N4 O4 S
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CBNB,
       CHEMCATS, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, PROUSDDR,
       RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
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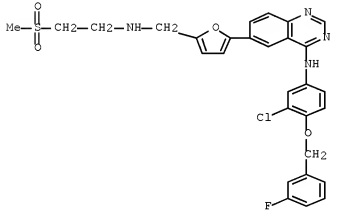


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             242 REFERENCES IN FILE CA (1907 TO DATE)
               4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             253 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> d his l7
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     (FILE 'HCAPLUS' ENTERED AT 10:04:29 ON 28 JAN 2008)
L7           253 S L5

=> d que l7
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "4-QUINAZOLINAMINE, N-(3-CHLO
                 RO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL
                 )ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L7           253 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5


=> d his l10

     (FILE 'HCAPLUS' ENTERED AT 10:04:29 ON 28 JAN 2008)
L10           28 S L7 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d que l10
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "4-QUINAZOLINAMINE, N-(3-CHLO
                 RO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL
                 )ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L7           253 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L10           28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND (AY<2004 OR PY<2004 OR
                 PRY<2004)
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These answers are covered in answer L30 (compound search related to cancer treatment)

***** QUERY RESULTS *****
(ELECTED SPECIES 1 AND 2 TOGETHER)

⇨ d his l8

(FILE 'HCAPLUS' ENTERED AT 10:04:29 ON 28 JAN 2008)
L8 1 S L6 AND L7

=> d que l8
L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON "BENZENESULFONAMIDE, 5-((4-((1,2-DIMETHYL-1H-BENZIMIDAZOL-5-YL)METHYLAMINO)-2-PYRIMIDINYL)AMINO)-2-METHYL-"/CN
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON "4-QUINAZOLINAMINE, N-(3-CHLORO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL)ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L6 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
L7 253 SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L8 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND L7

⇨ d l8 ibib ab

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1196402 HCAPLUS Full-text
DOCUMENT NUMBER: 143:452849
TITLE: Pyrimidine derivatives and quinazoline derivatives for cancer treatment
INVENTOR(S): Mullin, Robert John; Gilmer, Tona M.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Kumar, Rakesh
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105094	A2	20051110	WO 2005-US12337	20050412
WO 2005105094	A3	20060615		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1755394	A2	20070228	EP 2005-735666	20050412
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, LV				
JP 2007532658	T	20071115	JP 2007-508465	20050412
US 2007208023	A1	20070906	US 2006-599967	20061016
PRIORITY APPLN. INFO.:			US 2004-563285P	P 20040416
			US 2004-605288P	P 20040827

WO 2005-US12337 W 20050412

OTHER SOURCE(S): MARPAT 143:452849

AB A method for treating cancer is described including administration of a pyrimidine derivative and a quinazoline derivative Also described is a pharmaceutical composition including the same. Compound preparation is included.

***** QUERY RESULTS *****

(ELECTED SPECIES # 2 AND CANCER TREATMENT)

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   (13)  d his l30

     (FILE 'HCAPLUS' ENTERED AT 10:04:29 ON 28 JAN 2008)
L30          24 S L25 OR L29

   (13)  d que l30
L5            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "4-QUINAZOLINAMINE, N-(3-CHLO
                RO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL
                )ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L7          253 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L11      538951 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NEOPLASM+OLD,NT/CT
L12       94573 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARCINOMA/CT
L13       27398 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "COMBINATION CHEMOTHERAPY"+UF/
                CT
L14        7349 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COMB? (L) PHARMAC?/OBI
L15      574067 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (CODRUG# OR COADMIN? OR
                CONCOMITANT? OR CONCURRENT? OR BLEND? OR MIXTURE?)/OBI
L16        4809 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG DELIVERY SYSTEMS+OLD/CT
                (L) COMB?
L17       43372 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG INTERACTIONS+OLD,NT/CT
L18      258414 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ANTITUMOR AGENTS"+OLD,UF/CT
L19      827880 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CANCER# OR NEOPLASM? OR
                CARCINOMA OR TUMOR# OR TUMOUR#
L20      538951 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 OR L12
L22      643684 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L13 OR L14 OR L15 OR L16 OR
                L17)
L23         124 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L22
L24         120 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 AND (L18 OR L19 OR L20)
L25           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND (AY<2004 OR PY<2004
                OR PRY<2004)
L27         244 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND (L18 OR L19 OR L20)
L28          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND (AY<2004 OR PY<2004
                OR PRY<2004)
L29          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 NOT L25
L30          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 OR L29


=> d his l54

     (FILE 'MEDLINE, BIOSIS, DRUGU, BIOTECHNO, EMBASE' ENTERED AT 10:28:55 ON
     28 JAN 2008)
L54          28 S L52 OR L45

   (13)  d que l54
L5            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "4-QUINAZOLINAMINE, N-(3-CHLO
                RO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL
                )ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L15      574067 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (CODRUG# OR COADMIN? OR
                CONCOMITANT? OR CONCURRENT? OR BLEND? OR MIXTURE?)/OBI
L37         1013 SEA L5
L39     13128318 SEA (DRUG# OR PRODRUG# OR PHARMA? OR CHEMOTHERAP?)
L42       216675 SEA (TREAT# OR TREATMENT# OR TREATING# OR PREVENT? OR INHIB?)
                (2W) (CANCER# OR NEOPLASM? OR TUMOR# OR TUMOUR#)
L43         184 SEA L37 AND L42
L44         182 SEA L43 AND L39
L45          27 SEA L44 AND (AY<2004 OR PY<2004 OR PRY<2004)
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L46        1001 SEA L37 AND (L15 OR (COMBINAT? (W) CHEMOTHERAP? OR THERAP? OR
                TREATMENT# OR PHARMAC?))
L47         102 SEA L46 AND (AY<2004 OR PY<2004 OR PRY<2004)
L52          28 SEA L47 AND L42
L54          28 SEA L52 OR L45


   (13)  dup rem l30 l54
FILE 'HCAPLUS' ENTERED AT 10:52:51 ON 28 JAN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'BIOSIS' ENTERED AT 10:52:51 ON 28 JAN 2008
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FILE 'EMBASE' ENTERED AT 10:52:51 ON 28 JAN 2008
Copyright © 2008 Elsevier B.V. All rights reserved.
PROCESSING COMPLETED FOR L30
PROCESSING COMPLETED FOR L54
L57           51 DUP REM L30 L54 (1 DUPLICATE REMOVED)
                 ANSWERS '1-24' FROM FILE HCAPLUS
                 ANSWER '25' FROM FILE BIOSIS
                 ANSWERS '26-51' FROM FILE EMBASE

   (13)  d l57 1-24 ibib ed abs hitstr hitind; d l57 25-51 ibib ab hitind

L57  ANSWER 1 OF 51  HCAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2003:8967  HCAPLUS  Full-text
DOCUMENT NUMBER:          139:62338
TITLE:                    Small molecule tyrosine kinase inhibitors: clinical
                          development of anticancer agents
AUTHOR(S):                Laird, A. Douglas; Cherrington, Julie M.
CORPORATE SOURCE:         SUGEN, Inc., South San Francisco, CA, 94080, USA
SOURCE:                   Expert Opinion on Investigational Drugs (2003
                          ), 12(1), 51-64
                          CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER:                Ashley Publications Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
ED   Entered STN:  07 Jan 2003
AB   A review.  Numerous small mol. Synthetic tyrosine kinase inhibitors are in
     clin. Development for the treatment of human cancers.  These fall into three
     broad categories: inhibitors of the epidermal growth factor receptor tyrosine
     kinase family (e.g., Iressa and Tarceva), inhibitors of the split kinase
     domain receptor tyrosine kinase subgroup (e.g., PTK787/ZK 222584 and SU11248)
     and inhibitors of tyrosine kinases from multiple subgroups (e.g., Gleevec).
     In addition, agents targeting other tyrosine kinases implicated in cancer,
     such as Met, Tie-2 and Src, are in preclin. Development.  As experience is
     gained in the clinic, it has become clear that unleashing the full therapeutic
     potential of tyrosine kinase inhibitors will require patient preselection,
     better assays to guide dose selection, knowledge of mechanism-based side
     effects and ways to predict and overcome drug resistance.
IT   231277-92-2, GW-572016
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (small mol. Tyrosine kinase inhibitors and clin. Development of
        anticancer agents)
RN   231277-92-2  HCAPLUS
CN   4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-
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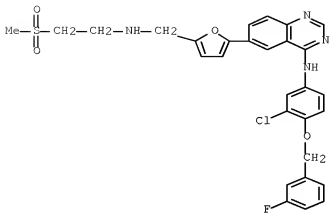
[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



CC 1-0 (Pharmacology)
Section cross-reference(s): 13
IT Antitumor agents
(resistance to; small mol. Tyrosine kinase inhibitors and clin. Development of anticancer agents)
IT Antitumor agents
Human
(small mol. Tyrosine kinase inhibitors and clin. Development of anticancer agents)
IT 111358-88-4, CEP-701 120685-11-2, PKC-412 152459-95-5, Imatinib 183319-69-9, OSI-774 184475-35-2, Iressa 187724-61-4, PKI-166 212142-18-2, PTK 787 220127-57-1, Gleevec 231277-92-2, GW-572016 252916-29-3, SU 6668 257933-82-7, EKB-569 289499-45-2, CI-1033 387867-13-2, MLN 518 402857-58-3, CEP 7055 443913-73-3, ZD 6474
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol. Tyrosine kinase inhibitors and clin. Development of anticancer agents)
REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 2 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1314363 HCAPLUS Full-text
DOCUMENT NUMBER: 144:57544
TITLE: Antibody drug conjugates and uses for cancer therapy
INVENTOR(S): Ebens, Allen J., Jr.; Jacobson, Frederic S.; Polakis, Paul; Schwall, Ralph H.; Sliwkowski, Mark X.; Spencer, Susan D.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 159
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005117986	A2	20051215	WO 2005-US18829	20050531
WO 2005117986	A3	20060615		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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ES 2253320	T3	20060601	ES 2001-127791	19980916 ←
NZ 528704	A	20050225	NZ 1999-528704	19990308 ←
CA 2450824	A1	20000420	CA 1999-2450824	19991005 ←
EP 1466977	A1	20041013	EP 2004-7618	19991202 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
NZ 523206	A	20041224	NZ 2000-523206	20000211 ←
NZ 523207	A	20041224	NZ 2000-523207	20000211 ←
NZ 523208	A	20041224	NZ 2000-523208	20000211 ←
NZ 523209	A	20041224	NZ 2000-523209	20000211 ←
CA 2481685	A1	20010308	CA 2000-2481685	20000824 ←
CA 2481691	A1	20010308	CA 2000-2481691	20000824 ←
CA 2481731	A1	20010308	CA 2000-2481731	20000824 ←
CA 2481756	A1	20010308	CA 2000-2481756	20000824 ←
CA 2481788	A1	20010308	CA 2000-2481788	20000824 ←
EP 1657251	A2	20060517	EP 2005-24036	20010601 ←
EP 1657251	A3	20060524		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, AL, TR				
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AU 759004	B2	20030403	AU 2001-57765	20010801 ←
CA 2420193	A1	20020228	CA 2001-2420193	20010823 ←
JP 2004520810	T	20040715	JP 2002-522275	20010823 ←
US 2003073129	A1	20030417	US 2001-946374	20010904 ←
US 2003207803	A1	20031106	US 2001-143026	20011019 ←
US 2003199021	A1	20031023	US 2001-13924	20011025 ←
EP 1397383	A2	20040317	EP 2001-990229	20011213 ←
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AU 778585	B2	20041209	AU 2002-14753	20020201 ←
CA 2449602	A1	20021219	CA 2002-2449602	20020403 ←
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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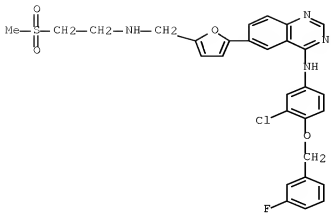
OTHER SOURCE(S): MARPAT 144:57544
ED Entered STN: 16 Dec 2005
AB The present invention relates to antibody-drug conjugate compds. With a formula of Ab-(L-D)p where 1 to 8 (p) maytansinoid drug moieties (D) are covalently linked by L to an antibody (Ab) which binds to an ErbB receptor, or which binds to one or more tumor-associated antigens or cell-surface receptors. These compds. May be used in methods of diagnosis or treatment of cancer, and other diseases and disorders.
IT 231277-92-2, Lapatinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody drug conjugates and uses for cancer therapy)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K047-48
ICS A61P035-00; G01N033-574
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15
IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-like protein 1; antibody drug conjugates and uses for cancer therapy)
IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ASLG659; antibody drug conjugates and uses for cancer therapy)
IT Cytokine receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAFF-R; antibody drug conjugates and uses for cancer therapy)
IT Chemokines
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BCA-1; antibody drug conjugates and uses for cancer therapy)
IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD72; antibody drug conjugates and uses for cancer therapy)
IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD79a; antibody drug conjugates and uses for cancer therapy)
IT Chemokine receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CXCR5; antibody drug conjugates and uses for cancer therapy)
IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ERBB2; antibody drug conjugates and uses for cancer therapy)
IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(GEDA; antibody drug conjugates and uses for cancer therapy)

IT Neuregulin receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HER3; antibody drug conjugates and uses for cancer therapy)

IT Neuregulin receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HER4; antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IRTA2 (Ig superfamily receptor translocation associated 2); antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MDP; antibody drug conjugates and uses for cancer therapy)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex), class II, subunit β; antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MSG783; antibody drug conjugates and uses for cancer therapy)

IT Mucins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC13; antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NCA; antibody drug conjugates and uses for cancer therapy)

IT Ion channel
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P2X5 (purinergic receptor P2X ligand-gated ion channel 5); antibody drug conjugates and uses for cancer therapy)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSCA (prostate stem cell antigen); antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSCA hlg; antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SH2 domain containing phosphatase anchor protein 1a; antibody drug conjugates and uses for cancer therapy)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(STEAP1 (six transmembrane epithelial antigen of prostate); antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Sema 5b; antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TENB2; antibody drug conjugates and uses for cancer therapy)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TMEFF2 (transmembrane protein with EGF-like and two follistatin domains 2); antibody drug conjugates and uses for cancer therapy)

IT Transport proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid transporter, cationic, E16, SLC7A5; antibody drug conjugates and uses for cancer therapy)

IT Angiogenesis inhibitors
Antitumor agents
Apoptosis
Bladder, neoplasm
Cytotoxicity
DNA sequences
Human
Immunohistochemistry
Kidney, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Protein sequences
Salivary gland, neoplasm
Stomach, neoplasm
Thyroid gland, neoplasm
Cdna sequences
(antibody drug conjugates and uses for cancer therapy)

IT Tumor antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody drug conjugates and uses for cancer therapy)

IT CA 125 (carbohydrate antigen)
Endothelin ETB receptors
neu (receptor)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody drug conjugates and uses for cancer therapy)

IT Drugs
(antibody-drug conjugate; antibody drug conjugates and uses for cancer therapy)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody-drug conjugate; antibody drug conjugates and uses for cancer therapy)

IT Prostate gland, neoplasm
(associated protein 1; antibody drug conjugates and uses for

cancer therapy)
IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(brevican; antibody drug conjugates and uses for cancer therapy)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric; antibody drug conjugates and uses for cancer therapy)
IT Intestine, neoplasm
(colon; antibody drug conjugates and uses for cancer therapy)
IT Intestine, neoplasm
(colorectal; antibody drug conjugates and uses for cancer therapy)
IT Uterus, neoplasm
(endometrium; antibody drug conjugates and uses for cancer therapy)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; antibody drug conjugates and uses for cancer therapy)
IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene B29; antibody drug conjugates and uses for cancer therapy)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized; antibody drug conjugates and uses for cancer therapy)
IT Drug delivery systems
(immunoconjugates; antibody drug conjugates and uses for cancer therapy)
IT Nucleic acid hybridization
(in situ, fluorescence; antibody drug conjugates and uses for cancer therapy)
IT Drug delivery systems
(infusions; antibody drug conjugates and uses for cancer therapy)
IT Cell proliferation
(inhibitory antibody; antibody drug conjugates and uses for cancer therapy)
IT Drug delivery systems
(injections, i.v.; antibody drug conjugates and uses for cancer therapy)
IT Drug delivery systems
(injections; antibody drug conjugates and uses for cancer therapy)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mesothelin; antibody drug conjugates and uses for cancer therapy)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal, 4D5; antibody drug conjugates and uses for cancer therapy)

IT Drug delivery systems
(parenterals; antibody drug conjugates and uses for cancer therapy)

IT Transport proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphate transporter, type II sodium-dependent phosphate transporter 3b; antibody drug conjugates and uses for cancer therapy)

IT Interleukin 20
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(receptor α; antibody drug conjugates and uses for cancer therapy)

IT Epidermal growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor; antibody drug conjugates and uses for cancer therapy)

IT Carcinoma
(teratocarcinoma, -derived growth factor; antibody drug conjugates and uses for cancer therapy)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(teratocarcinoma-derived; antibody drug conjugates and uses for cancer therapy)

IT Cation channel
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transient receptor potential; antibody drug conjugates and uses for cancer therapy)

IT Neoplasm
(treatment of; antibody drug conjugates and uses for cancer therapy)

IT Complement receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type 2; antibody drug conjugates and uses for cancer therapy)

IT Bone morphogenetic protein receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type IB; antibody drug conjugates and uses for cancer therapy)

IT Gene, microbial
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(v-erbB; antibody drug conjugates and uses for cancer therapy)

IT 295808-11-6 336196-29-3 400200-43-3 459580-14-4 479331-40-3 479331-41-4 479331-42-5 479475-04-2 479920-01-9 480096-56-8 480589-89-7 481152-11-8 481238-06-6, Protein (human gene CR2) 606652-60-2 624517-66-4 624643-08-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; antibody drug conjugates and uses for cancer therapy)

IT 140742-49-0, GenBank M11767 140958-83-4, GenBank M11761 292557-16-5, GenBank AK026467 331228-08-1, GenBank AF343662 331228-09-2, GenBank

AF343663 331228-10-5, GenBank AF343664 331228-11-6, GenBank AF343665 335573-94-9, GenBank AF369794 352847-85-9, GenBank AF397453 379653-70-0, GenBank AY065994 385236-46-4, GenBank AF043498 385342-41-6, GenBank AF116456 389185-35-7, GenBank M29541 392080-81-8, GenBank AF132600 441566-86-5, GenBank AL834187 441591-81-7, GenBank AK090423 441592-33-2, GenBank AK090475 493655-82-6, GenBank AK089756 512281-67-3, GenBank AY158090 606640-65-7, GenBank AY358085 606641-55-8, GenBank AY358130 606658-17-7, GenBank AY358907 730906-79-3, GenBank AY506558
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antibody drug conjugates and uses for cancer therapy)

IT 51-21-8, 5-FU 58-05-9, Leucovorin 4856-87-5 5132-30-9 28537-70-4, 1,4-Bis-maleimidobutane 53123-88-9, Rapamycin 61825-94-3, Oxaliplatin 64987-85-5, SMCC 71865-37-7 86099-06-1 112809-51-5, Letrozole 115597-84-7 129453-61-8, Fulvestrant 179324-69-7, Bortezomib 180288-69-1, Trastuzumab 183321-74-6, Erlotinib 184475-35-2, Gefitinib 189013-00-1 193275-84-2, Lonafarnib 212142-18-2, ZK222584 216974-75-3, Bevacizumab 220127-57-1, Imatinib mesylate 231277-92-2, Lapatinib 284461-73-0, Sorafenib 557795-19-4, Sutent
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody drug conjugates and uses for cancer therapy)

IT 140742-22-9, DNA (human gene CR2 protein Cdna) 243994-71-0 266667-01-0 280538-18-3, DNA (human gene PSCA) 295772-85-9 347837-10-9 369350-11-8 384463-70-1, GenBank M11730 389182-65-4 392100-56-0, DNA (human gene TENB2 protein Cdna) 392140-36-2, DNA (human protein ASLG659-specifying) 451738-59-3 508116-00-5, DNA (human gene LHFPL3 protein Cdna) 519942-34-8, DNA (human gene EDNRB protein Cdna) 606652-59-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; antibody drug conjugates and uses for cancer therapy)

L57 ANSWER 3 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:490384 HCAPLUS Full-text
DOCUMENT NUMBER: 143:42681
TITLE: Anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer
INVENTOR(S): Wang, Yan; Pachter, Jonathan A.; Bishop, Walter R.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005052005	A1	20050609	WO 2004-US38842	20041119 ←

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004292554	A1	20050609	AU 2004-292554	20041119	←
CA 2546664	A1	20050609	CA 2004-2546664	20041119	←
US 2005136063	A1	20050623	US 2004-993395	20041119	←
EP 1689782	A1	20060816	EP 2004-811545	20041119	←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU					
CN 1906214	A	20070131	CN 2004-80040801	20041119	←
JP 2007532478	T	20071115	JP 2006-541410	20041119	←
IN 2006CN01763	A	20070706	IN 2006-CN1763	20060519	←
MX 2006PA05779	A	20060714	MX 2006-PA5779	20060522	←
NO 2006002885	A	20060818	NO 2006-2885	20060620	←
PRIORITY APPLN. INFO.:			US 2003-524732P	P 20031121	←
			WO 2004-US38842	W 20041119	

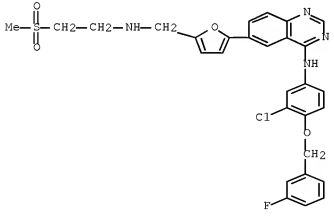
ED Entered STN: 09 Jun 2005

AB The present invention provides combinations including a binding composition, such as an anti-IGFR1 antibody, in association with a chemotherapeutic agent. The antibody is e.g. a human monoclonal antibody recognizing human IGFR-1, especially soluble IGFR-1. The chemotherapeutic agent is selected from a taxane, topoisomerase inhibitor, signal transduction inhibitor, cell cycle inhibitor, farnesyl protein transferase inhibitor, EGFR inhibitor, HER2 inhibitor, VEGFR inhibitor, MAP kinase inhibitor, MEK kinase inhibitor, AKT kinase inhibitor, Mtor inhibitor, etc. Methods for using the combinations to treat medical conditions, such as cancer, are also provided.

IT 231277-92-2, Lapatinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM C07K016-28
ICS A61K039-395; A61K031-00

CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 2, 3, 63
ST human IGFR1 monoclonal antibody chemotherapeutic agent combination therapy cancer
IT Animal cell line
(A2780; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Animal cell line
(MCF-7; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Animal cell line
(NCI-H322; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Kidney, neoplasm
(Wilms'; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Acromegaly
Antiestrogens
Atherosclerosis
Behcet's syndrome
Bladder, neoplasm
Bone, neoplasm
Combination chemotherapy
DNA sequences
Diarrhea
Drugs
Graves' disease
Human
Lung, neoplasm
Mammary gland, neoplasm
Molecular cloning
Multiple sclerosis
Myasthenia gravis
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Protein sequences
Psoriasis
Rheumatoid arthritis
Selective estrogen receptor modulators
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Insulin-like growth factor I receptors
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Antisense nucleic acids
neu (receptor)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Autoimmune disease

Inflammation
Thyroid gland, disease
(autoimmune thyroiditis; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Prostate gland, disease
(benign hyperplasia; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Hyperplasia
(benign prostatic; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Drug delivery systems
(carriers; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Uterus, neoplasm
(cervix, carcinoma; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Carcinoma
Uterus, neoplasm
(cervix; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Intestine, neoplasm
(colorectal; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Medical goods
(containers; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Artery, disease
(coronary, restenosis; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Blood vessel, disease
(endothelium; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Growth disorders, animal
(gigantism; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chain; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Cell cycle
Signal transduction, biological
(inhibitors; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Anthracyclines
Epidermal growth factor receptors
Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)
IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(light chain; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Containers
(medical; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Carcinoid
(metastatic; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Stabilizing agents
(microtubule; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulators; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Antibodies and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Synovial membrane, disease
(neoplasm, sarcoma; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Lung, neoplasm
(non-small-cell carcinoma; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Drug delivery systems
(parenterals; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Neoplasm
(pediatric; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Medicine
(pediatrics, cancer; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Carcinoma
(pulmonary non-small-cell; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Artery, disease
(restenosis; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Microtubule
(stabilizers or inhibitors; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Sarcoma
(synovial membrane; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Lupus erythematosus
(systemic; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT Endothelium
(vascular, disease; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 366017-09-6, TAK 165
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(TAK 165; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 853169-76-3P 853169-78-5P 853169-79-6P 853169-80-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 853169-81-0
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 280107-15-5P 628700-70-9P 628700-72-1P 628700-74-3P 628700-76-5P 628700-78-7P 628700-80-1P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 57-22-7, Vincristine 518-28-5, Podophyllotoxin 865-21-4, Vinblastine 1605-68-1D, Taxane, analogs and _acques. 7689-03-4, Camptothecin 10540-29-1, Tamoxifen 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 56420-45-2, Epirubicin 84449-90-1, Raloxifene 89778-26-7, Toremifene 97682-44-5, Irinotecan 114977-28-5, Docetaxel 116057-75-1, Idoxifene 123948-87-8, Topotecan 129453-61-8, Fulvestrant 152044-54-7, Epothilone B 180288-69-1, Trastuzumab 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, Acolbifene 183321-74-6, Erlotinib 184475-35-2, Gefitinib 187724-61-4, PKI-166 192185-72-1, Tipifarnib 193275-84-2, Lonafarnib 198480-55-6, Pipendoxifene 198481-32-2, Bazedoxifene 205923-56-4, Cetuximab 219989-84-1, BMS-247550 231277-92-2, Lapatinib 257933-82-7, EKB-569 267243-28-7, Canertinib 280578-49-6, BMS-310705 339177-26-3, ABX-EGF 352233-83-1, HMR 3339 383432-38-0, CP 724714 698387-09-6, HKI-272 853112-60-4, ZK 186619
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 9039-48-9, Aromatase 61912-98-9, IGF 67763-96-6, IGF-1 67763-97-7, IGF-2 80449-01-0, Topoisomerase 115926-52-8, PI3 kinase 131384-38-8, Farnesyl protein transferase 139691-76-2, Raf kinase 140879-24-9, Proteasome 142243-02-5 142805-58-1, MAPK/ERK kinase 148640-14-6, AKT kinase 150428-23-2 171715-28-9, MTOR kinase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

IT 853168-30-6P 853169-77-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

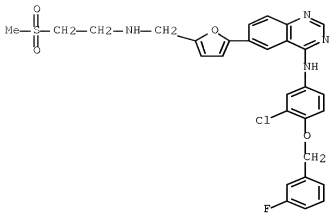
IT 37221-79-7, VIP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor secreting; anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 4 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:470251 HCAPLUS Full-text
DOCUMENT NUMBER: 143:19957
TITLE: Combination therapy comprising a cyclooxygenase 2 (COX-2) inhibitor and an antineoplastic agent for treatment or prevention of neoplasia
INVENTOR(S): Masferrer, Jaime L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 317 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005048942	A2	20050602	WO 2004-US38019	20041115 ←
WO 2005048942	A3	20060330		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005227929	A1	20051013	US 2004-989192	20041115 ←
PRIORITY APPLN. INFO.:			US 2003-519701P P	20031113 ←

ED Entered STN: 02 Jun 2005
AB A method for treating or preventing neoplasia or a neoplasia-related disorder in a subject is provided, the method comprising administering to the subject an effective amount of a combination comprising a COX-2 inhibitor and an antineoplastic agent.
IT 231277-92-2, GW-572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
IT Lymphoma
(AIDS-related; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Reproductive system, neoplasm
(Bartholin's gland carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Bone, neoplasm
(Ewing's sarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(Ewing's; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(Kaposi's; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Melanoma
(MART-1 melanoma vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Skin, neoplasm
(Merkel cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Tumor antigens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NY-ESO-1, ESO-1:157-165 peptide vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Skin, neoplasm
(T-cell lymphoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Lymphoproliferative disorders
(Waldenstrom's macroglobulinemia; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Kidney, neoplasm
(Wilms'; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Carcinoma
(adenocarcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(adenoid cystic carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Liver, neoplasm
(adenoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(adenosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(adenosquamous; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(adrenocortical; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neuroglia, neoplasm
(allogeneic glioma vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Intestine, neoplasm
(anus; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neuroglia, neoplasm
(astrocytoma, cerebral; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neuroglia, neoplasm
(astrocytoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Skin, neoplasm
(basal cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(basal cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neuroglia, neoplasm
(brain stem; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(bronchial; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Ovary, neoplasm
(carcinoma, serous; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Adrenal cortex, neoplasm
Bronchi, neoplasm
Capillary vessel
Meninges
Pancreatic islet of Langerhans, neoplasm
(carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(carcinosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(cartilage chondrosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Carcinoma
(cavernous cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neoplasm
(childhood; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(cholangiocarcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Biliary tract, neoplasm
(cholangioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Cartilage, neoplasm
(chondrosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Brain, neoplasm
Meninges
(choroid plexus carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(choroid plexus; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Intestine, neoplasm
(colon, allogeneic colon cancer vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Intestine, neoplasm
(colon; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Intestine, neoplasm
(colorectal; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Lymphoma
(cutaneous T-cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Adenoma
Antitumor agents
Bile duct, neoplasm
Bladder, neoplasm
Brain, neoplasm
Carcinoid
Combination chemotherapy
Cyclooxygenase 2 inhibitors
Drug delivery systems
Esophagus, neoplasm
Fowlpox virus
Gallbladder, neoplasm
Gene therapy
Hodgkin's disease
Human
Human papillomavirus 16
Immunotherapy
Kidney, neoplasm
Larynx, neoplasm
Leukemia
Liver, neoplasm
Lung, neoplasm
Lymphocyte
Mammary gland, neoplasm

Melanoma
Mouth, neoplasm
Multiple myeloma
Myelodysplastic syndromes
Myeloproliferative disorders
Neoplasm
Neuroglia, neoplasm
Nose, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Parathyroid gland, neoplasm
Pharynx, neoplasm
Pheochromocytoma
Pituitary gland, neoplasm
Prophylaxis
Prostate gland, neoplasm
Radiotherapy
Sarcoma
Thyroid gland, neoplasm
Vaccines
Vagina, neoplasm
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Antisense oligonucleotides
Interleukin 2
Phosphorothioate oligonucleotides
Tricyclic compounds
Tumor necrosis factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Adenoma
(cystadenoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Ovary, neoplasm
(endodermal sinus tumor; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Uterus, neoplasm
(endometrium, adenocarcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Uterus, neoplasm
(endometrium, stromal sarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Blood vessel, neoplasm
(endothelioma, hemangioendothelioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Brain, neoplasm
(ependyma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neoplasm
(gastrinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neoplasm
(germ cell, extragonadal; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neoplasm

(germ cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neuroglia, neoplasm
(glioblastoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Pancreatic islet of Langerhans, neoplasm
(glucagonoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Blood vessel, neoplasm
(hemangioblastoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Blood vessel, neoplasm
(hemangioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Liver, neoplasm
(hepatic adenomatosis; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Adenoma
(hepatic; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Carcinoma
(hepatocellular, fibrolamellar; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Carcinoma
(hepatocellular; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Liver, neoplasm
(hepatoma, fibrolamellar; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Liver, neoplasm
(hepatoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neuroglia, neoplasm
(hypothalamic and visual pathway; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Lymphoma
(idiotypic KLH lymphoma vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Pancreatic islet of Langerhans, neoplasm
(insulinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neoplasm
(intraepithelial; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Lung, neoplasm
(large-cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Myoma
Sarcoma
(leiomyosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Drug delivery systems
(liposomes; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Central nervous system, neoplasm
(lymphoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination

for treatment or prevention of neoplasia)
IT Brain, neoplasm
(medulloblastoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Thymus gland, neoplasm
(medulloepithelioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Mesothelium, neoplasm
(mesothelioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neoplasm
(metastasis; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(metastatic; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Mucous membrane
(mucoepidermoid carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Skin, neoplasm
(mycosis fungoides; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Multiple myeloma
(myeloma-derived idiotypic antigen vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Tumor antigens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(myeloma-derived idiotypic antigen vaccine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(nasopharyngeal; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Pharynx, neoplasm
(nasopharynx, carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Astrocyte
(neoplasm, astrocytoma, cerebral; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Astrocyte
(neoplasm, astrocytoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Gamete and Germ cell
(neoplasm, extragonadal; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Oligodendrocyte
(neoplasm, oligodendroglioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Gamete and Germ cell
Lip
Penis
Trophoblast

Urethra
(neoplasm; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Nerve, neoplasm
(neuroblastoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Nervous system, neoplasm
(neuroectoderm, pineal and supratentorial; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Nerve, neoplasm
(neuroepithelial adenocarcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Lymphoma
(non-Hodgkin's; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neuroglia, neoplasm
(oligodendroglioma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Bone, neoplasm
Sarcoma
(osteosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(ovarian, serous; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(pancreatic islet; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(papillary adenocarcinoma, serous; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Respiratory system, neoplasm
(paranasal sinus; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(pharyngeal squamous cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Brain, neoplasm
(pinealoma, pineal cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(pseudosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Lung, neoplasm
(pulmonary and pleuropulmonary blastoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(pulmonary large-cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(pulmonary small-cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Intestine, neoplasm
(rectum; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Kidney, neoplasm
(renal cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(renal cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Eye, neoplasm
(retinoblastoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(rhabdomyosarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Uterus, neoplasm
(sarcoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Lung, neoplasm
(small-cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Intestine, neoplasm
(small; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Animal tissue, disease
(soft, neoplasm, carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Neoplasm
(soft-tissue, carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Pharynx, neoplasm
(squamous cell carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(squamous cell, interepithelial; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(squamous cell; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Mesothelium, neoplasm
(submesothelial carcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Thymus gland, neoplasm
(thymoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Chorion, neoplasm
(trophoblastic; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma
(uterine endometrial adenocarcinoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Sarcoma
(uterine; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)
IT Carcinoma

(verrucous; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Neoplasm
(vipoma; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT Reproductive system, neoplasm
(vulva; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

IT 74-79-3D, L-Arginine, monomethyl _acques. 103-82-2D, Phenylacetic acid, _acques. 254-04-6D, Benzopyran, _acques. 355-25-9, NC 100100 646-08-2, β-Alethine 1400-61-9, Nystatin 1821-33-6 2353-33-5, 5-Aza-2'-deoxycytidine 5072-26-4, Buthionine sulfoximine 7689-03-4D, Camptothecin, glycoconjugate 9005-49-6, Dalteparin, biological studies 9014-42-0, RH-TPO 9074-87-7, Carboxypeptidase G2 18472-51-0, Oramed 19388-87-5, Taurolidine 33069-62-4, Paclitaxel 41941-56-4, Tocladesine 82855-09-2, Combretastatin 82952-64-5, Trimetrexate glucuronate 89778-26-7, GTx 006 97919-22-7 108560-70-9, Gallium maltolate 115427-51-5, INX-3280 118694-43-2, ILX 23-7553 128517-07-7 134774-45-1, Rasburicase 149882-10-0, Lurtotecan 152044-54-7, Epothilone B 152044-54-7D, Epothilone B, analogs 152459-95-5, Imatinib 156053-89-3, ADL 8-2698 160237-25-2, BMS-184476 162011-90-7, Rofecoxib 162635-04-3, CCI-779 169590-42-5, Celecoxib 170729-80-3, Aprepitant 172481-83-3, BMS 188797 173424-77-6, VNP-40101M 173937-91-2, Atrasentan 181695-72-7, Valdecoxib 186348-23-2, BAY 59-8862 188968-51-6, Cilengitide 191732-72-6, CDC 501 192391-48-3, Bexxar 192658-64-3 192819-27-5, CDC-801 195533-53-0, T-138067 195987-41-8 198470-84-7, Parecoxib 198470-85-8, Parecoxibsodium 198480-55-6, ERA 923 202409-33-4, Etoricoxib 205923-56-4, Cetuximab 209783-80-2, MS-275 209810-58-2, Aranesp 216503-58-1, BEC2 216974-75-3, Bevacizumab 219527-63-6, Repifermin 219989-84-1, BMS-247550 220578-59-6, Mylotarg 220991-20-8, Lumiracoxib 227619-96-7, CP-461 231277-92-2, GW-572016 236391-66-5, GTI 2040 236391-67-6, GTI 2501 246861-96-1, SB 251353 257933-82-7, EKB-569 259188-38-0, BMS-275291 261944-52-9 263351-82-2 267243-28-7 284461-73-0, BAY 439006 288392-69-8, MEDI-507 289499-45-2, CI-1033 321309-50-6, NC-100150 340014-19-9, Melacine 380907-94-8, Cytotoxin SS1(dsFv)-PE38 (synthetic) 428438-54-4, SPD 424 439153-64-7, CP 609754 447471-67-2, MG-98 543726-73-4, IMC 1C11 623174-20-9, ILX 651 791096-83-8, SD 01 845680-07-1, Lapuleucel-T 848866-33-1, T 900607 852286-49-8 852834-17-4, PK 412 852834-62-9D, TNT 1B, I131 labeled 852834-90-3, KSB 309 852834-96-9, SB 310 852835-00-8, NBI 3001 852835-01-9, APC 8020 852835-30-4, RK 0202 852835-36-0, SR 29142 852835-43-9, Stemgen 852835-52-0, ALVAC B 7.1 852835-53-1, GnRH Pharmaccine 852836-15-8, Rv-MUC 1 852836-20-5, CaPVax
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

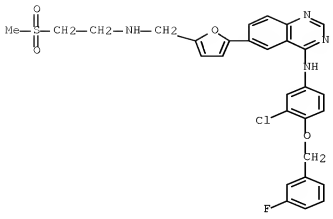
IT 51110-01-1, Somatostatin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin-secreting tumor; cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

L57 ANSWER 5 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:451189 HCAPLUS Full-text
DOCUMENT NUMBER: 142:476214
TITLE: Erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment
INVENTOR(S): Dev, Inderjit Jumar; Gilmer, Tana Morgan; Rhodes,

Cliford Nelson, III; Tansik, Robert L.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046678	A1	20050526	WO 2004-US37027	20041105 ←
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1682123	A1	20060726	EP 2004-810446	20041105 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
JP 2007510667	T	20070426	JP 2006-538522	20041105 ←
US 2007161665	A1	20070712	US 2006-595691	20060505 ←
PRIORITY APPLN. INFO.:			US 2003-518212P P	20031107 ←
			WO 2004-US37027 W	20041105

OTHER SOURCE(S): MARPAT 142:476214
ED Entered STN: 27 May 2005
AB The invention discloses a method for treating cancer in a mammal, as well as pharmaceutical combinations useful in such treatment. In particular, the method relates to a cancer treatment method that includes administering an erb family inhibitor and a PI3K and/or Akt inhibitor to a mammal suffering from a cancer. Preparation of inhibitors is described.
IT 231277-92-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K031-415
ICS A61K031-535
CC 1-6 (Pharmacology)
Section cross-reference(s): 28, 63
ST erb family PI3K Akt inhibitor prepn cancer treatment
IT Head and Neck, neoplasm
Head and Neck, neoplasm
(carcinoma; erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT Mammary gland, neoplasm
(ductal carcinoma; erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT Antitumor agents
Apoptosis
Combination chemotherapy
Human
Neoplasm
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(erb family; erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT Carcinoma
Carcinoma
(head and neck; erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT Carcinoma
(mammary ductal; erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT Drug interactions
(synergistic; erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT 115926-52-8, PI3 kinase 148640-14-6, Akt kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)
IT 231277-92-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)

IT 607373-66-0P 607373-68-2P 842144-79-0P 842146-05-8P 842146-10-5P 842146-12-7P 842146-18-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)

IT 19545-26-7, Wortmannin 154447-36-6 388082-77-7 388082-79-9, GW 589522 388082-81-3, GW 583340 852023-81-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)

IT 75-04-7, Ethylamine, reactions 98-80-6, Phenylboronic acid 105-56-6, Ethyl cyanoacetate 124-40-3, Dimethylamine, reactions 372-09-8, Cyanoacetic acid 1796-84-5, 4-Ethoxy-3-nitropyridine 2516-47-4, Cyclopropanemethylamine 3680-02-2, Methyl vinyl sulfone 4152-09-4, N-Benzylethylenediamine 4945-54-4 7803-49-8, Hydroxylamine, reactions 24424-99-5, Di-tert-Butyldicarbonate 31872-61-4, 4-Methoxy-3-nitropyridine hydrochloride 31872-62-5, 4-Methoxy-3-nitropyridine 49773-20-8 58885-58-8 63503-60-6, 3-Chlorophenylboronic acid 75178-87-9 94602-04-7, 4-Ethoxy-3-nitropyridine hydrochloride 109384-19-2 123855-51-6 202272-67-1 231278-84-5 320337-16-4 320337-48-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)

IT 1633-43-8P 562825-95-0P 607370-99-0P 607371-01-7P 607371-03-9P 607373-60-4P 607373-65-9P 607373-67-1P 842143-89-9P 842143-97-9P 842143-99-1P 842144-00-7P 842144-03-0P 842144-04-1P 842144-05-2P 842144-06-3P 842144-07-4P 842144-08-5P 842144-57-4P 842146-03-6P 842146-04-7P 852023-72-4P 852023-73-5P 852023-74-6P 852023-75-7P 852023-76-8P 852023-77-9P 852023-78-0P 852023-79-1P 852023-80-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)

IT 202272-68-2P 319917-44-7P 319917-46-9P 320337-12-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(erb family inhibitor and PI3K and/or Akt inhibitor for cancer treatment)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 6 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:158866 HCAPLUS Full-text
DOCUMENT NUMBER: 142:254573
TITLE: Assessment of the efficiency of solid tumor treatment by a dual EGFR/erbB2 tyrosine kinase inhibitor from the levels and relative localization of phosphorylated ERK1/2 or AKT kinases
INVENTOR(S): Bacus, Sarah S.; Spector, Neil Lee
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005017493	A2	20050224	WO 2004-US26434	20040810 ←
WO 2005017493	A3	20071206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA				
EP 1664716	A2	20060607	EP 2004-781163	20040810 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2007059785	A1	20070315	US 2006-568251	20060214 ←
PRIORITY APPLN. INFO.:			US 2003-495325P	P 20030815 ←
			WO 2004-US26434	W 20040810

ED Entered STN: 24 Feb 2005

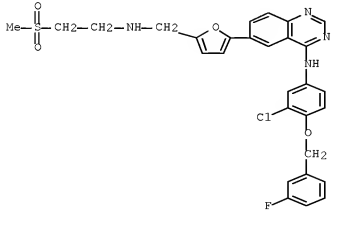
AB Biomarkers may be used in the treatment of cancer, and as an aid in clin. Decision making regarding which anti-cancer therapy to use in a particular patient. Described herein are methods of assessing whether a subject with an EGFR-expressing or erbB2-expressing solid tumor is suitable for treatment with a dual EGFR/erbB2 tyrosine kinase inhibitor, by assessing the relative localization of phosphorylated protein kinase ERK1/2 or phosphorylated protein kinase AKT in tumor cells, and/or assessing pre-treatment tumor cell levels of ErbB2.

IT 231277-92-2, GW572016

RL: PAC (Pharmacological activity); BIOL (Biological study) (assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM G01N
CC 1-6 (Pharmacology)
Section cross-reference(s): 14
ST solid tumor anticancer EGFR erbB2 inhibitor ERK AKT phosphorylation
IT Signal transduction, biological
(GW572016 inhibits erbB2 tyrosine phosphorylation and downstream activation of Erk1/2 and EGF-induced activation of ERK1/2 and AKT in carcinoma)
IT Antitumor agents
Bladder, neoplasm
Carcinoma
Cell nucleus
Cytoplasm
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Immunohistochemistry
Kidney, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Ovary, neoplasm
Prognosis
Tumor markers
(assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT Epidermal growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT Intestine, neoplasm
(colon; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT Neoplasm
Neoplasm
(head and neck; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT Phosphorylation, biological
(protein; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT Neoplasm
(solid; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT Blood plasma
(steady-state concentration of anticancer drug; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)
IT 62229-50-9, EGF
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GW572016 blocks EGF-induced activation of ERK1/2 and AKT in carcinoma; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and

localization of phosphorylated ERK1/2 or AKT kinases)

IT 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 137632-09-8, ErbB2 tyrosine kinase 142243-02-5 148640-14-6, AKT kinase
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)

IT 231277-92-2, GW572016
RL: PAC (Pharmacological activity); BIOL (Biological study)
(assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)

IT 180288-69-1, Herceptin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effect of GW572016 on Erk1/2 activation state differ from that of Herceptin; assessment of efficiency of solid tumor treatment by dual EGFR/erbB2 tyrosine kinase inhibitor from levels and localization of phosphorylated ERK1/2 or AKT kinases)

L57 ANSWER 7 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:158541 HCAPLUS Full-text
DOCUMENT NUMBER: 142:254570
TITLE: Dosing schedule for erbB2 anticancer agents
INVENTOR(S): Bhattacharya, Samit Kumar; Connell, Richard Damian; Moyer, James Dale; Jani, Jitesh Pranlal; Noe, Dennis Alan; Steyn, Stefanus Johannes
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016347	A1	20050224	WO 2004-IB2580	20040806 ←
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004264726	A1	20050224	AU 2004-264726	20040806 ←
CA 2536140	A1	20050224	CA 2004-2536140	20040806 ←
EP 1658080	A1	20060524	EP 2004-744217	20040806 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1838959	A	20060927	CN 2004-80023705	20040806 ←
BR 2004013745	A	20061024	BR 2004-13745	20040806 ←
JP 2007502807	T	20070215	JP 2006-523695	20040806 ←
SG 135193	A1	20070928	SG 2007-6063	20040806 ←
US 2005119288	A1	20050602	US 2004-919831	20040817 ←

IN 2006DN00271	A	20070817	IN 2006-DN271		20060116	←
MX 2006PA01989	A	20060517	MX 2006-PA1989		20060220	←
NO 2006001252	A	20060516	NO 2006-1252		20060317	←
PRIORITY APPLN. INFO.:			US 2003-495919P	P	20030818	←
			WO 2004-IB2580	W	20040806	

OTHER SOURCE(S): MARPAT 142:254570

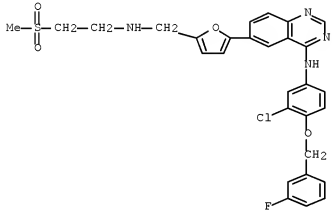
ED Entered STN: 24 Feb 2005

AB The invention discloses methods for treating overexpression of erbB2 in a mammal in need of treatment by administering a therapeutically effective amount of a first inhibitor of an erbB2 receptor and then, after an interval of less than 24 h, administering to the mammal 1-6 therapeutically effective amts. Of the same or different inhibitor of the erbB2 receptor. The invention also discloses a slow daily infusion of the erbB2 inhibitor. The overexpression of the erbB2 receptor can result in abnormal cell growth and lead to cancer. By the methods of the invention, the efficacy and safety of the inhibitors is increased. The invention further discloses kits for facilitating the dose administration method of the invention.

IT 231277-92-2, GW-572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erbB2 anticancer agent dosing schedule)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K031-517
ICS A61K031-506; A61P035-00; A61K031-00

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

ST cancer treatment erbB2 inhibitor dosing

IT Neoplasm
(FRE/erbB2; erbB2 anticancer agent dosing schedule)

IT Mammary gland, neoplasm
Ovary, neoplasm
(adenocarcinoma; erbB2 anticancer agent dosing schedule)

IT Antitumor agents
Combination chemotherapy
Cytotoxic agents
Human
Neoplasm

Pharmacokinetics
Vaccines
(erbB2 anticancer agent dosing schedule)
IT Carcinoma
(mammary adenocarcinoma; erbB2 anticancer agent dosing schedule)
IT Carcinoma
(ovarian adenocarcinoma; erbB2 anticancer agent dosing schedule)
IT Drug interactions
(synergistic; erbB2 anticancer agent dosing schedule)
IT 53123-88-9, Rapamune 62229-50-9D, Epidermal growth factor, fusion protein with P64K 139504-50-0D, Maytansinoid DM1, Trastuzumab conjugates 159351-69-6, RAD 001 160212-35-1 162635-04-3, CCI-779 180288-69-1, Trastuzumab 180288-69-1D, Trastuzumab, maytansinoid DM1 conjugates 183321-74-6, Erlotinib 184475-35-2, Iressa 205923-56-4, Cetuximab 231277-92-2, GW-572016 257933-82-7, EKB-569 289499-45-2 339152-71-5, MDX 210 339177-26-3, ABX-EGF 339186-68-4, EMD-72000 366017-09-6, TAK 165 383430-46-4 383430-52-2 383430-55-5 383430-69-1 383430-82-8 383430-98-6 383430-99-7 383431-07-0 383431-08-1 383431-09-2 383431-59-2 383431-72-9 383431-80-9 383432-02-8 383432-38-0, CP 724714 383432-58-4 383432-65-3 383432-75-5 383432-99-3 383433-00-9 383433-03-2 383433-08-7 383433-12-3 383433-40-7 383433-57-6 454691-40-8, FD-137 474436-65-2, Herzyme 497839-62-0, AEE 788 572924-54-0, AP 23573 713145-83-6, DAB 720 845512-02-9 845512-04-1 845512-22-3 845512-23-4 845679-64-3, IDM 1 845679-80-3, ME 103 845679-97-2, YMB 1001 845680-07-1, Lapuleucel-T 845681-01-8, ADL 681 845681-48-3, D 69491 845681-62-1, EHT 102 845682-29-3, HuMax-DGFr 845682-32-8, ME 104 845682-35-1, MR 1-1 845682-38-4, SC 100 845682-42-0, YMB 1005 845882-21-5, B 17
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erbB2 anticancer agent dosing schedule)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 8 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:120678 HCAPLUS Full-text
DOCUMENT NUMBER: 142:191228
TITLE: Treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment
INVENTOR(S): Spector, Neil Lee; Xia, Wenle
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011607	A2	20050210	WO 2004-US24888	20040802 ←
WO 2005011607	A3	20050721		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1653986 A2 20060510 EP 2004-779830 20040802 ←

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR

US 2006204966 A1 20060914 US 2006-567012 20060201 ←

PRIORITY APPLN. INFO.: US 2003-491752P P 20030801 ←

WO 2004-US24888 W 20040802

ED Entered STN: 11 Feb 2005

AB The truncated ErbB2 receptor (p95ErbB2) is shown to differ from the full-length ErbB2 receptor in its association with other ErbB receptors. The truncated receptor preferentially associated with ErbB3, whereas full length ErbB2 heterodimerizes with either EGFR or ErbB3. Consistent with p95ErbB2 heterodimerization with ErbB3, it is shown that heregulin (an ErbB3 ligand) stimulates p95ErbB2 phosphorylation in breast cancer cell lines. Described herein are methods of identifying patients suitable for treatment with a p95ErbB2 inhibitor, and methods of treating such patients. GW572016, a p95ErbB2 inhibitor, inhibited both p95ErbB2 and p185ErbB2 in breast cancer xenografts.

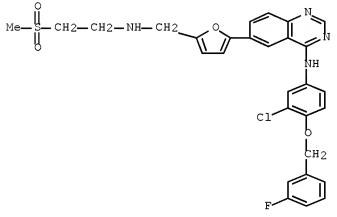
IT 231277-92-2, GW572016

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as p95 ErbB2 inhibitor; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

Section cross-reference(s): 9, 14

ST cancer expressing p95 ErbB2 treatment inhibitor; breast cancer expressing p95 ErbB2 treatment inhibitor; truncated ErbB2 receptor expressing cancer detn treatment; antitumor GW572016 p95 ErbB2 inhibitor

IT Neuregulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HER3, truncated ErbB2 preferentially associating with; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Carcinoma
Mammary gland, neoplasm
(adenocarcinoma; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Samples
(anal. Of; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Drug resistance
(antitumor, to trastuzumab, GW572016 treatment in relation to; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Head and Neck, neoplasm
Head and Neck, neoplasm
(carcinoma; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Intestine, neoplasm
(colon; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Intestine, neoplasm
(colorectal; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Protein motifs
(extracellular domain, of ErbB2, determination of; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Neoplasm
(granular cell; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Carcinoma
Carcinoma
Neoplasm
Neoplasm
(head and neck; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Carcinoma
(mammary adenocarcinoma; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Bone, neoplasm
Lymph node, neoplasm
(metastasis; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; treatment of cancers expressing p95 ErbB2 with

p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Combination chemotherapy
(of p185 ErbB2 inhibitor and p95 ErbB2 inhibitor; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Phosphorylation, biological
(protein, of truncated ErbB2, heregulin stimulation of, in breast cancer cell lines; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Kidney, neoplasm
(renal cell carcinoma; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Carcinoma
(renal cell; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Antitumor agents
(resistance to, to trastuzumab, GW572016 treatment in relation to; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Neoplasm
(solid; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Antitumor agents
Bladder, neoplasm
Blood analysis
Carcinoma
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Immunoblotting
Immunohistochemistry
Lung, neoplasm
Mammary gland, neoplasm
Neoplasm
Ovary, neoplasm
(treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT Neuregulin 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(truncated ErbB2 phosphorylation stimulation by, in breast cancer cell lines; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT 137632-07-6, Protein kinase Erk1 148640-14-6, AKT kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GW572016 inhibition of EGF and heregulin activation of; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

IT 62229-50-9, EGF
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GW572016 inhibition of Erk1/2 and AKT activation by; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)
IT 180288-69-1, Trastuzumab
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (as p185 ErbB2 inhibitor, treating cancer resistant to; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)
IT 231277-92-2, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (as p95 ErbB2 inhibitor; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)
IT 137632-08-7, Protein kinase Erk2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)
IT 388082-77-7
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)

L57 ANSWER 9 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:902075 HCAPLUS Full-text
DOCUMENT NUMBER: 141:361105
TITLE: Methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof
INVENTOR(S): Chan-Hui, Po-Ying; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja
PATENT ASSIGNEE(S): Aclara Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 32
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091384	A2	20041028	WO 2004-US9715	20040330 ←
WO 2004091384	A3	20051229		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,

SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004126818 A1 20040701 US 2003-623057 20030717 ←
US 7105308 B2 20060912
AU 2004229348 A1 20041028 AU 2004-229348 20040330 ←
CA 2521077 A1 20041028 CA 2004-2521077 20040330 ←
EP 1613205 A2 20060111 EP 2004-759064 20040330 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
CN 1836051 A 20060920 CN 2004-80014942 20040330 ←
JP 2006523314 T 20061012 JP 2006-509479 20040330 ←
BR 2004008961 A 20061031 BR 2004-8961 20040330 ←
AU 2004267420 A1 20050303 AU 2004-267420 20040810 ←
CA 2535510 A1 20050303 CA 2004-2535510 20040810 ←
WO 2005019470 A2 20050303 WO 2004-US25945 20040810 ←
WO 2005019470 A3 20050609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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EP 1673399 A2 20060628 EP 2004-780731 20040810 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
BR 2004013471 A 20061017 BR 2004-13471 20040810 ←
JP 2007502417 T 20070208 JP 2006-523311 20040810 ←

PRIORITY APPLN. INFO.:
US 2003-459888P P 20030401 ←
US 2003-623057 A 20030717 ←
US 2003-494482P P 20030811 ←
US 2003-508034P P 20031001 ←
US 2003-512941P P 20031020 ←
US 2003-523258P P 20031118 ←
US 2002-398724P P 20020725 ←
WO 2004-US9715 W 20040330
WO 2004-US25945 W 20040810

ED Entered STN: 28 Oct 2004

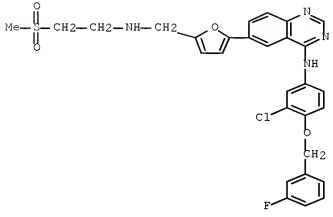
AB The invention is directed to a new class of biomarker in patient samples comprising _acques of ErbB cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. Of one or more _acques of ErbB cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a cancer in a specimen from an individual by correlating measurements of amts. Of one or more _acques of ErbB cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a cancer, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. Having releasable mol. Tags that are specific for multiple components of one or more types of receptor _acques. After binding, mol. Tags are released and separated from the assay mixture for anal.

IT 231277-92-2, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61B

CC 2-10 (Mammalian Hormones)

ST ErbB membrane receptor complex cancer biomarker enzymic cleavage treatment

IT Neuregulin 1
Platelet-derived growth factors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(-activated receptor; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Cell membrane
(ErbB receptor complexes at; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Neuregulin receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HER3, heterodimers with Her1, PI3K, SHC, IGF1R, PDGFR, p95Her2 and EGFRvIII; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Neuregulin receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HER4, homodimers and heterodimers with Her2; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Proteins
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(SRC-like adapter, src homol. 2 dimers with Her1, Her2 and Her3; methods for detection of ErbB cell surface receptor complexes as

cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Epidermal growth factor receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TGF-a-erbB complex; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Fibrosis
(aberrant, cell surface receptor complexes-associated; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Protein degradation
(cleavage of receptor complexes for detection; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Intestine, neoplasm
(colorectal; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Platelet-derived growth factor receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(complexes, heterodimers with Her1, Her2 and Her3; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Antitumor agents
(_acque-acting drugs as; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Neuroglia, neoplasm
(glioblastoma; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Insulin-like growth factor I receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(heterodimers with Her1, Her2 and Her3; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Dimerization
(homo- and hetero-, of ErbB receptors; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Epidermal growth factor receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(homodimers and heterodimers with Her3, PI3K, SHC, IGF1R, PDGFR, p95Her2 and EGFRvIII; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT neu (receptor)
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(homodimers and heterodimers with Her4, PI3K, SHC, IGF1R, PDGFR, p95Her2 and EGFRvIII; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Ligands
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(labeled, binding to receptors in complexes; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Proteins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(labeled, ligands for receptors in complexes; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Biomarkers
Diagnosis
Human
Mammary gland, neoplasm
Neoplasm
Ovary, neoplasm
Prognosis
Prostate gland, neoplasm
Tumor markers
(methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Phosphorylation, biological
(receptor, ligand-activated; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Probes (nucleic acid)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(with enzymic activity to cleave receptor complexes; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT Transforming growth factors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(α-, -activated receptor; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT 62229-50-9, Epidermal growth factor
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(-activated receptor; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT 115926-52-8, PI3 kinase
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(heterodimers with Her1, Her2 and Her3; methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

IT 180288-69-1, Herceptin 183319-69-9, Tarceva 184475-35-2, Iressa 187724-61-4, PKI 166 205923-56-4, Erbitux 231277-92-2, GW572016 257933-82-7, EKB-569 289499-45-2, CI-1033 339151-96-1, MDX 447 339177-26-3, ABX-EGF 339186-68-4, EMD 72000 780758-10-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

L57 ANSWER 10 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:100947 HCAPLUS Full-text
DOCUMENT NUMBER: 140:139486
TITLE: Method of treating cancer

INVENTOR(S): Potter, David A.
PATENT ASSIGNEE(S): Advanced Research & Technology Institute at Indiana University, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004010937	A2	20040205	WO 2003-US23437	20030728 ←
WO 2004010937	A3	20040527		
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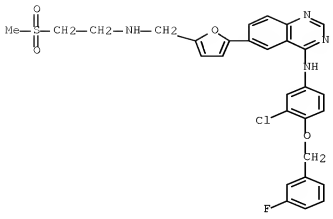
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003256847	A1	20040216	AU 2003-256847	20030728 ←
US 2004167139	A1	20040826	US 2003-629045	20030728 ←
US 2007009593	A1	20070111	US 2006-451875	20060613 ←
PRIORITY APPLN. INFO.:			US 2002-399573P	P 20020726 ←
			US 2003-629045	B1 20030728 ←
			WO 2003-US23437	W 20030728 ←

ED Entered STN: 08 Feb 2004
AB Methods for treating cancer are described here. The methods include administering to an HIV-neg. patient an m-calpain inhibitor such as ritonavir. Ritonavir or other m-calpain inhibitors can also be co-administered with other therapeutic agents such as a Cox-2 inhibitor, a taxane, or a proteasome inhibitor. Methods for determining whether a patient will respond to a particular method of treatment are also described herein.
IT 231277-92-2, GW 572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating cancer)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
Section cross-reference(s): 63
ST antitumor ritonavir taxane calpain COX2 inhibitor combination cancer therapy
IT Multidrug resistance proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BCRP (breast cancer resistance protein); treating cancer)
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells); treating cancer)
IT Drug resistance
(antitumor; treating cancer)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binds and antagonizes EGF receptor or erbB2; treating cancer)
IT Intestine, neoplasm
(colon; treating cancer)
IT Spectrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fodrins, α-; treating cancer)
IT Neoplasm
Neoplasm
(head and neck; treating cancer)
IT Cell differentiation
(inducers; treating cancer)
IT Epidermal growth factor receptors
P-glycoproteins
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treating cancer)
IT Lung, neoplasm
(non-small-cell carcinoma; treating cancer)
IT Anti-inflammatory agents
(nonsteroidal; treating cancer)
IT Drug delivery systems
(prodrugs; treating cancer)

IT Carcinoma
(pulmonary non-small-cell; treating cancer)
IT Antitumor agents
(resistance to; treating cancer)
IT Drug interactions
(synergistic; treating cancer)
IT Analgesics
Antiemetics
Antitumor agents
Brain, neoplasm
Drug delivery systems
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Human immunodeficiency virus 1
Lung, neoplasm
Mammary gland, neoplasm
Melanoma
Nausea
Ovary, neoplasm
Pain
Pancreas, neoplasm
Physiological saline solutions
Prostate gland, neoplasm
Signal transduction, biological
Stomach, neoplasm
(treating cancer)
IT Multidrug resistance proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treating cancer)
IT Interleukin 2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(treating cancer)
IT Taxanes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating cancer)
IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(α; treating cancer)
IT 78990-62-2, Calpain
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, m-; treating cancer)
IT 140879-24-9, Organelle, proteasome 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treating cancer)
IT 23214-92-8, Doxorubicin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(normal and liposomal; treating cancer)
IT 142243-02-5, ERK kinase 148640-14-6, Akt kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treating cancer)
IT 56092-81-0, Ionomycin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(treating cancer)
IT 50-07-7, Mitomycin-c 50-18-0, Cyclophosphamide 50-24-8, Prednisolone
50-76-0, Dactinomycin 51-21-8, 5-Fluorouracil 57-22-7, Vincristine
58-05-9, Leucovorin 59-05-2, Methotrexate 147-94-4, Cytarabine

148-82-3, Melphalan 564-25-0, Doxycycline 671-16-9, Procarbazine 865-21-4, Vinblastine 3778-73-2, Ifosfamide 4291-63-8, 2-CDA 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13311-84-7, Flutamide 15663-27-1, Cisplatin 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 53714-56-0, Leuprolide 56420-45-2, Epirubicin 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 71486-22-1, Vinorelbine 84449-90-1, Raloxifene 89778-26-7, Toremifene 97682-44-5, Irinotecan 112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1 127779-20-8, Saquinavir 129453-61-8, Fulvestrant 150378-17-9 155213-67-5 159878-27-0 161814-49-9 169590-42-5, Celecoxib 174722-31-7, Rituximab 179324-69-7, VELCADE 183319-69-9, Tarceva 184475-35-2, Iressa 192725-17-0 205923-56-4, C225 216503-57-0, Campath 231277-92-2, GW 572016 257933-82-7, EKB569 289499-45-2, CI-1033 339177-26-3, ABX-EGF
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating cancer)

L57 ANSWER 11 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:995727 HCAPLUS Full-text
DOCUMENT NUMBER: 141:420611
TITLE: ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB _acque acting drugs
INVENTOR(S): Chan-hui, Po-Ying; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U.S. Ser. No. 623,057.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 32
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2004229380	A1	20041118	US 2004-813412	20040330	←
US 2003013126	A1	20030116	US 2002-154042	20020521	←
US 7255999	B2	20070814			
US 2004126818	A1	20040701	US 2003-623057	20030717	←
US 7105308	B2	20060912			
AU 2004267420	A1	20050303	AU 2004-267420	20040810	←
CA 2535510	A1	20050303	CA 2004-2535510	20040810	←
WO 2005019470	A2	20050303	WO 2004-US25945	20040810	←
WO 2005019470	A3	20050609			

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1673399 A2 20060628 EP 2004-780731 20040810 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
BR 2004013471 A 20061017 BR 2004-13471 20040810 ←
JP 2007502417 T 20070208 JP 2006-523311 20040810 ←
PRIORITY APPLN. INFO.: US 2002-154042 A2 20020521 ←
US 2003-623057 A2 20030717 ←
US 2003-494482P P 20030811 ←
US 2003-508034P P 20031001 ←
US 2003-512941P P 20031020 ←
US 2003-523258P P 20031118 ←
US 2001-292548P P 20010521 ←
US 2001-334901P P 20011024 ←
US 2002-398724P P 20020725 ←
WO 2004-US25945 W 20040810

ED Entered STN: 19 Nov 2004

AB The invention is directed to a new class of biomarker in patient samples comprising heterodimers of Her cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. Of one or more heterodimers of ErbB or Her cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a cancer in a specimen from an individual by correlating measurements of amts. Of one or more heterodimers of ErbB cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a cancer, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. Having releasable mol. Tags that are specific for multiple components of one or more types of receptor _acques. After binding, mol. Tags are released and separated from the assay mixture for anal.

IT 231277-92-2, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB _acque-acting drugs)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)

IC ICM G01N033-543
INCL 436518000
CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 1, 15
ST ErbB heterodimer biomarker cancer diagnosis treatment
IT Animal tissue
Bioassay
Biomarkers
Cell membrane
Diagnosis
Dimerization
Epithelium
Fluorescence
Human
Mammary gland, neoplasm
Neoplasm
Ovary, neoplasm
Prognosis
Prostate gland, neoplasm
(ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB _acque-acting drugs)
IT Diagnosis
(cancer; ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB _acque-acting drugs)
IT Intestine, neoplasm
(colorectal; ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB _acque-acting drugs)
IT Antitumor agents
(_acque-acting drugs; ErbB heterodimers as biomarkers for determining disease
status and for selecting patients for treatment with ErbB _acque-acting drugs)
IT 180288-69-1, Herceptin 231277-92-2, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB _acque-acting drugs)

L57 ANSWER 12 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:999609 HCAPLUS Full-text
DOCUMENT NUMBER: 141:420612
TITLE: ErbB surface receptor complexes as biomarkers in determining disease
INVENTOR(S): Chan-Hui, Po-Ying; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-part of U.S. Ser. No. 623,057.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 32
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004229294	A1	20041118	US 2004-813417	20040330	←
US 2003013126	A1	20030116	US 2002-154042	20020521	←
US 7255999	B2	20070814			
US 2004126818	A1	20040701	US 2003-623057	20030717	←
US 7105308	B2	20060912			
AU 2004267420	A1	20050303	AU 2004-267420	20040810	←
CA 2535510	A1	20050303	CA 2004-2535510	20040810	←
WO 2005019470	A2	20050303	WO 2004-US25945	20040810	←
WO 2005019470	A3	20050609			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1673399	A2	20060628	EP 2004-780731	20040810	←

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

BR 2004013471	A	20061017	BR 2004-13471	20040810	←
JP 2007502417	T	20070208	JP 2006-523311	20040810	←
US 2005130238	A1	20050616	US 2005-41041	20050121	←
US 2005170438	A1	20050804	US 2005-41029	20050121	←
US 2005170439	A1	20050804	US 2005-41073	20050121	←

PRIORITY APPLN. INFO.:	US 2002-154042	A2	20020521 ←
	US 2003-459888P	P	20030401 ←
	US 2003-623057	A2	20030717 ←
	US 2003-494482P	P	20030811 ←
	US 2003-508034P	P	20031001 ←
	US 2003-512941P	P	20031020 ←
	US 2003-523258P	P	20031118 ←
	US 2001-292548P	P	20010521 ←
	US 2001-334901P	P	20011024 ←
	US 2002-398724P	P	20020725 ←
	US 2004-813417	A1	20040330
	WO 2004-US25945	W	20040810

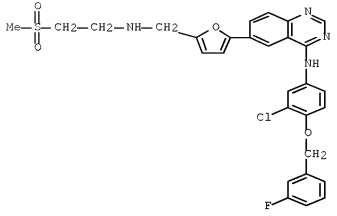
ED Entered STN: 19 Nov 2004

AB The invention is directed to a new class of biomarker in patient samples comprising _acques of ErbB cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. Of one or more _acques of ErbB cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a cancer in a specimen from an individual by correlating measurements of amts. Of one or more _acques of ErbB cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a cancer, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. Having releasable mol. Tags that are specific for multiple components of one or more types of receptor _acques. After binding, mol. Tags are released and separated from the assay mixture for anal.

IT 231277-92-2, GW572016

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ErbB-dimer acting drugs; ErbB surface receptor complexes as biomarkers in determining disease)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM G01N033-53
ICS G01N033-567
INCL 435007200
CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 1, 15
IT Animal tissue
Antitumor agents
Bioassay
Biomarkers
Cell membrane
Diagnosis
Dimerization
Disease, animal
Epithelium
Fibrosis
Fluorescence
Human
Mammary gland, neoplasm
Neoplasm
Ovary, neoplasm
Prognosis
Prostate gland, neoplasm
(ErbB surface receptor complexes as biomarkers in determining disease)
IT Diagnosis
(cancer; ErbB surface receptor complexes as biomarkers in determining disease)
IT Intestine, neoplasm
(colorectal; ErbB surface receptor complexes as biomarkers in determining disease)
IT 180288-69-1, Herceptin 183319-69-9, Tarceva 184475-35-2, Iressa 187724-61-4, PKI 166 205923-56-4, Erbitux 231277-92-2, GW572016 257933-82-7, EKB-569 289499-45-2, CI-1033 339151-96-1, MDX 447 339177-26-3, ABX-EGF 339186-68-4, EMD72000 780758-10-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

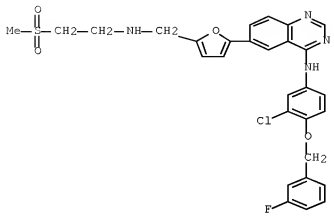
(Biological study); USES (Uses)
(ErbB-dimer acting drugs; ErbB surface receptor complexes as biomarkers in determining disease)

L57 ANSWER 13 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:533970 HCAPLUS Full-text
DOCUMENT NUMBER: 141:65088
TITLE: Methods and compositions for the prevention or treatment of neoplasia comprising a COX-2 inhibitor in combination with an epidermal growth factor receptor antagonist
INVENTOR(S): Masferrer, Jaime
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 470,951.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004127470	A1	20040701	US 2003-651916	20030829 ←
EP 1522313	A1	20050413	EP 2004-26577	19991222 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO, CY				
WO 2005037259	A2	20050428	WO 2004-US27574	20040825 ←
WO 2005037259	A3	20050804		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004210578	A1	20041007	AU 2004-210578	20040910 ←
PRIORITY APPLN. INFO.:			US 1998-113786P	P 19981223 ←
			US 1999-470951	B2 19991222 ←
			US 1999-385214	A 19990827 ←
			AU 2000-25936	A3 19991222 ←
			EP 1999-968939	A3 19991222 ←
			US 2003-651916	A 20030829 ←

ED Entered STN: 02 Jul 2004
AB The present invention relates to a novel method of preventing and/or treating neoplasia disorders in a subject that is in need of such prevention or treatment by administering to the subject at least one COX-2 inhibitor in combination with an EGF receptor antagonist. Compns., pharmaceutical compns. And kits are also described.
IT 231277-92-2, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as EGFR antagonist; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K031-60
ICS A61K031-415; A61K031-19
INCL 514165000; 514406000; 514471000; 514420000; 514569000; 514570000
CC 1-6 (Pharmacology)
Section cross-reference(s): 7, 63
IT Lymphoma
(AIDS-related, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Reproductive system
(Bartholin's gland, neoplasm, carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Gland
(Bartholin's, neoplasm, carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Angiogenesis inhibitors
Antitumor agents
Drug delivery systems
Human
Neoplasm
Prophylaxis
(COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Bone, neoplasm
(Ewing's sarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Sarcoma
(Ewing's, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Sarcoma
(Kaposi's, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or

treatment of neoplasia)

IT Skin, neoplasm
(T-cell lymphoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Lymphoproliferative disorders
(Waldenstrom's macroglobulinemia, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Kidney, neoplasm
(Wilms', treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Melanoma
(acral lentiginous, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(adenocarcinoma, neuroepithelial, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(adenocarcinoma, papillary serous adenocarcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(adenocarcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(adenoid cystic, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Liver, neoplasm
(adenoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Sarcoma
(adenosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(adenosquamous, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(adrenocortical, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Intestine
(anus, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Neuroglia, neoplasm
(astrocytoma, cerebral, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Neuroglia, neoplasm
(astrocytoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for

prevention or treatment of neoplasia)

IT Skin, neoplasm
(basal cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(basal cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Lung, neoplasm
(biphasic blastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(bronchial, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Adrenal cortex, neoplasm
Bronchi, neoplasm
Pancreatic islet of Langerhans, neoplasm
(carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Sarcoma
(carcinosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Sarcoma
(cartilage chondrosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Development, mammalian postnatal
(child, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(cholangiocarcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Biliary tract, neoplasm
(cholangioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Cartilage, neoplasm
(chondrosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Brain, neoplasm
Meninges
(choroid plexus carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(choroid plexus, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Intestine, neoplasm
(colon, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Intestine, neoplasm
(colorectal, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Lymphoma
(cutaneous T-cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Adenoma
(cystadenoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Meninges
(disease, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Leukemia
(disorders related to, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(endodermal sinus tumor, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Uterus, neoplasm
(endometrium, adenocarcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(fibrolamellar, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(focal nodular hyperplasia, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(gastrinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Ovary, neoplasm
(germ cell tumor, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(germ cell, extragonadal, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(germ cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neuroglia, neoplasm
(glioblastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Pancreatic islet of Langerhans, neoplasm
(glucagonoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Blood vessel, neoplasm
(hemangioblastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Blood vessel, neoplasm
(hemangioendothelioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Blood vessel, neoplasm
(hemangioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Liver, neoplasm
(hepatic adenomatosis, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Adenoma
(hepatic, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Carcinoma
(hepatocellular, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Liver, neoplasm
(hepatoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Pharynx, neoplasm
(hypopharyngeal cancer, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Brain, neoplasm
(hypothalamic and visual pathway glioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Pancreatic islet of Langerhans, neoplasm
(insulinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Neoplasm
(intraepithelial, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Drug delivery systems
(kits; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Lung, neoplasm
(large-cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Myoma
Sarcoma
(leiomyosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Melanoma
(lentigo maligna, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Central nervous system, neoplasm
(lymphoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Brain, neoplasm
(medulloblastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Brain, neoplasm
(medulloepithelioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Eye, neoplasm
(melanoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Nervous system, disease
(meningeal, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Skin, neoplasm
(merkel cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Lung, neoplasm
(metastasis, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Carcinoma
(mucoepidermoid carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Skin, neoplasm
(mycosis fungoides, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Carcinoma
(nasopharyngeal, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Pharynx, neoplasm
(nasopharynx, carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Astrocyte
(neoplasm, astrocytoma, cerebral, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Astrocyte
(neoplasm, astrocytoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Capillary vessel
(neoplasm, carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Gamete and Germ cell
(neoplasm, extragonadal, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Gamete and Germ cell
Lip
Oligodendrocyte
Penis
Pineal gland
Urethra
(neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Nerve, neoplasm
(neuroblastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Melanoma
(nodular, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Lymphoma
(non-Hodgkin's, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Lung, neoplasm
(non-small-cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Bone, neoplasm
Sarcoma
(osteosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Carcinoma
(pancreatic islet, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pancreatic polypeptide, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Respiratory system
(paranasal sinus, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Carcinoma
(pharyngeal squamous cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Lung, neoplasm
(pleuropulmonary blastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Drug delivery systems
(prodrugs, of COX-2 selective inhibitors; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Sarcoma
(pseudosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)
IT Carcinoma

(pulmonary large-cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(pulmonary non-small-cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(pulmonary small-cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Kidney, neoplasm
(renal cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(renal cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Eye, neoplasm
(retinoblastoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Sarcoma
(rhabdomyosarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Uterus, neoplasm
(sarcoma, stromal sarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Uterus, neoplasm
(sarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(serous, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Intestine, neoplasm
(small, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Lung, neoplasm
(small-cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Animal tissue, disease
(soft, neoplasm, carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Neoplasm
(soft-tissue, carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Pharynx, neoplasm
(squamous cell carcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma

(squamous cell, interepithelial, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(squamous cell, metastasis, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(squamous cell, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Brain
(stem, neoplasm, glioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Neoplasm
(submesothelial, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Melanoma
(superficial spreading, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Brain, neoplasm
(supratentorial primitive neuroectodermal, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Thymus gland, neoplasm
(thymoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Adenoma
Bile duct, neoplasm
Bladder, neoplasm
Brain, neoplasm
Carcinoid
Carcinoma
Esophagus, neoplasm
Gallbladder, neoplasm
Hodgkin's disease
Kidney, neoplasm
Larynx, neoplasm
Liver, neoplasm
Lung, neoplasm
Lymphoma
Mammary gland, neoplasm
Melanoma
Mesothelium, neoplasm
Mouth, neoplasm
Multiple myeloma
Myelodysplastic syndromes
Myeloproliferative disorders
Neuroglia, neoplasm
Nose, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Parathyroid gland, neoplasm
Pheochromocytoma
Pituitary gland, neoplasm
Prostate gland, neoplasm

Sarcoma
Spinal cord, neoplasm
Thyroid gland, neoplasm
Vagina, neoplasm
(treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(uterine endometrial adenocarcinoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Sarcoma
(uterine, stromal sarcoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Sarcoma
(uterine, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Eye, neoplasm
(uvea, melanoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Carcinoma
(verrucous, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Neoplasm
(vipoma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Neuroglia, neoplasm
(visual pathway glioma, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT Reproductive system
(vulva, neoplasm, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT 51803-78-2, Nimesulide 71125-38-7, Meloxicam 80937-31-1, Flosulide 123653-11-2, NS-398 123663-49-0, T-614 139226-28-1, Darbufelone 158089-95-3, S 2474 158205-05-1, L-745337 162011-90-7, Rofecoxib 162054-19-5, SC-58125 168434-89-7, CT 3 169590-41-4, Deracoxib 169590-42-5, Celecoxib 179382-91-3, RS 57067 180200-68-4, JTE-522 181695-72-7, Valdecoxib 189955-09-7, L-784512 190967-35-2, RWJ-63556 197438-48-5, BMS-347070 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 220991-20-8, Lumiracoxib 266320-83-6, ABT-963 329306-31-2, S-33516 346670-87-9, CS 502 (pharmaceutical) 485397-24-8, SD-8381 485397-25-9, LAS-34555 485397-26-0, LAS-34475 630395-06-1, SVT-2016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as COX-2 selective inhibitor; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT 95-16-9D, Benzothiazole, compds. 100-42-5D, Styrene, substituted 253-66-7D, Cinnoline, _acques. 253-82-7D, Quinazoline, compds. 446-72-0, Genistein 446-72-0D, Genistein, conjugates with epidermal growth factor 458-37-7, Curcumin 15018-66-3D, 4-Aminoquinazoline, compds. 34157-83-0, Celastrol 34923-95-0D, compds. 37270-94-3, Platelet factor 4 62229-50-9D, EGF, fusion proteins with toxin

75706-12-6, SU-101 80497-65-0, Muellerian-inhibiting hormone 104326-05-8, BBR 1611 117147-70-3, Amphiregulin 118409-60-2, RG-50864 129298-91-5, AGM-1470 134615-37-5, Reveromycin A 134633-29-7, Tecogalan sodium 138147-78-1, RC-3095 138989-57-8, RG-14620 140674-76-6, AG-957 140674-79-9, AG 514 145588-13-2, BE 23372M 145588-13-2D, BE 23372M, _acques. 145915-58-8, CGP-52411 145915-60-2, CGP 53353 146426-40-6, Flavopiridol 147159-51-1, TT-232 149286-90-8, RG-13022 150779-71-8, SDZ-LAP-977 150977-36-9, Bromelain 151013-48-8, AG-568 152459-94-4, CGP-53716 152459-95-5 153436-53-4, AG 1478 153436-54-5, SU 5271 153436-54-5D, analogs 153436-70-5, ZM 105180 154387-41-4, NSC 675967 156177-59-2, CEP-751 162382-68-5, RC-3940-II 164003-59-2, VRCTC-310 171179-06-9, PD 158780 173458-56-5, CGP-59326 176915-62-1, CGP-62706 179343-17-0, PD-089828 180288-69-1, Trastuzumab 183319-69-9 183321-74-6, Erlotinib 183488-70-2, CEP-2563 184475-35-2, ZD-1839 185077-23-0, PI 88 186519-23-3D, compds. 187724-61-4, PKI-166 194423-15-9, PD-168393 196612-93-8, BIBX 1382 197359-31-2 202196-59-6, GW5289 202271-41-8, GW0277 202272-68-2, GW2974 202272-69-3, GW9263 204005-46-9, SU-5416 205923-56-4, C225 212141-54-3, CGP-79787 212142-18-2, PTK 787 220127-57-1, Imatinib mesylate 231277-92-2, GW572016 257933-82-7, EKB-569 259672-35-0, BIBX1522 267243-28-7 289499-45-2, CI-1033 305820-76-2, PD-173956 339151-96-1, EMD 82633 339152-71-5, MDX-210 339177-26-3, ABX-EGF 339186-66-2, EMD-55900 339186-68-4, EMD-72000 339526-85-1, MDX-260 378223-57-5 386744-54-3, GW 4263 386744-56-5, GW 9525 403850-97-5, ZM-254530 437755-78-7, GW-2016 713078-32-1 713145-03-0, PD 171026 713145-04-1, PD 090560 713145-05-2, EMD 6200 713145-06-3, BAB 447 713145-70-1, H 447 713145-71-2, ZD 1838 713145-74-5, CGP 59326B 713145-75-6, CGP 74321 713145-76-7, CGP 76627 713145-77-8, DWP 408 713145-80-3, S 96-8045 713145-81-4, GEM 220 713145-82-5, AR 639 713145-83-6, DAB 720 713145-86-9, OLX 103 713145-89-2, NX 278L 713145-95-0, PD 169450 713146-03-3, QX 101 713146-04-4, FCE 26806 713146-05-5, CGP 60261 713146-06-6, PD 159973 713146-07-7, GW 282974 713146-08-8, CP 292597 713146-09-9, GW 7072X 713146-10-2, FCE 27119 713146-11-3, PD 154233 713146-12-4, PD 151514 713146-13-5, KW 6151 713146-16-8, C 1033 713146-17-9, GW 211 713146-18-0, GW 5949 713146-20-4, PD 13530 713146-21-5, CGP 5211

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as EGFR antagonist; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

IT 51110-01-1, Somatostatin

RL: BSU (Biological study, unclassified); BIOL (Biological study) (tumors secreting, treatment or prevention of; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

L57 ANSWER 14 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2004:2613 HCAPLUS Full-text
DOCUMENT NUMBER:	140:53400
TITLE:	Cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy
INVENTOR(S):	Bacus, Sarah S.
PATENT ASSIGNEE(S):	Ventana Medical Systems, Inc., USA; Smithkline Beecham Corporation
SOURCE:	PCT Int. Appl., 35 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000101	A2	20031231	WO 2003-US19697	20030619 ←
WO 2004000101	A3	20060908		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003247602	A1	20040106	AU 2003-247602	20030619 ←
PRIORITY APPLN. INFO.:			US 2002-389795P	P 20020619 ←
			US 2002-432811P	P 20021211 ←
			WO 2003-US19697	W 20030619 ←

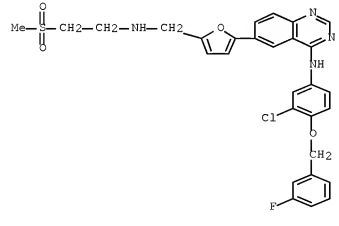
ED Entered STN: 02 Jan 2004

AB This invention provides methods for determining or predicting response to HER1/HER2-directed cancer therapy in an individual. The methodol. Of the invention includes assaying a tumor sample with one or more reagents that detect expression and/or activation of predictive biomarkers for cancer, e.g. growth factor receptors, growth factor receptor ligands, and growth factor receptor-related downstream signaling mols.

IT 231277-92-2, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61B
CC 1-6 (Pharmacology)

Section cross-reference(s): 14

ST tumor marker HER1 HER2 antitumor therapy response; growth factor receptor HER1 HER2 antitumor therapy response; ligand growth factor receptor HER1 HER2 antitumor therapy response; signaling mol HER1 HER2 antitumor therapy response

IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Neuregulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HER3; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Carcinoma
Mammary gland, neoplasm
(adenocarcinoma; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Antitumor agents
Cell cycle
Human
Neoplasm
Ovary, neoplasm
Sarcoma
Tumor markers
(cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Epidermal growth factor receptors
Epidermal growth factor receptors
Growth factor receptors
Insulin-like growth factor receptors
Neuregulin 1
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Head and Neck, neoplasm
Head and Neck, neoplasm
(carcinoma; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Signal transduction, biological
(growth factor receptor-related downstream signaling mols.; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Ligands
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(growth factor receptor; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Carcinoma
Carcinoma
(head and neck; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Carcinoma

(mammary adenocarcinoma; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Mammary gland, neoplasm
(metastasis; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α-; cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

IT 79079-06-4, HER1 kinase 137632-07-6, Erk1 kinase 137632-08-7, Erk2 kinase 137632-09-8, HER2 kinase 142243-02-5, ERK kinase 148640-14-6, Akt kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

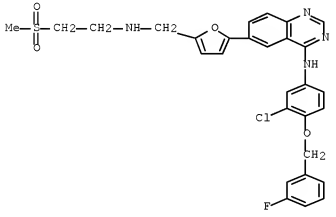
IT 231277-92-2, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

L57 ANSWER 15 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:2612 HCAPLUS Full-text
DOCUMENT NUMBER: 140:53399
TITLE: Predictive markers in cancer therapy
INVENTOR(S): Bacus, Sarah S.; Herrle, Myra R.; Kirk, L. Edward; Spector, Neil L.; Stocum, Michael T.; Xia, Wenle
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000094	A2	20031231	WO 2003-US12739	20030424 ←
WO 2004000094	A3	20070614		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BE, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA				
AU 2003235470	A1	20040106	AU 2003-235470	20030424 ←
EP 1810034	A2	20070725	EP 2003-724213	20030424 ←
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR, LT, LV				
US 2006094068	A1	20060504	US 2005-529922	20050330 ←
PRIORITY APPLN. INFO.:			US 2002-389795P P	20020619 ←

US 2002-432811P P 20021211 ←
US 2002-432943P P 20021211 ←
US 2003-451978P P 20030303 ←
WO 2003-US12739 W 20030424 ←

ED Entered STN: 02 Jan 2004
AB Mol. Markers useful in medicine response tests are provided, as an aid in determining whether an individual subject's tumor is responding to treatment with EGF and/or erbB2 inhibitors. Markers include phosphorylated ERK protein.
IT 231277-92-2, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(predictive markers in cancer therapy)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61B
CC 1-6 (Pharmacology)
Section cross-reference(s): 2
ST EGFR erbB2 inhibitor antitumor marker GW572016 tumor apoptosis signaling
IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; predictive markers in cancer therapy)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERBB1; predictive markers in cancer therapy)
IT Gene, animal
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ERBB2; predictive markers in cancer therapy)
IT Carcinoma
(adenocarcinoma; predictive markers in cancer therapy)
IT Intestine, neoplasm
(colon; predictive markers in cancer therapy)
IT Neoplasm
Neoplasm
(head and neck; predictive markers in cancer therapy)
IT Antitumor agents

Apoptosis
Bladder, neoplasm
Blood plasma
Carcinoma
Cell cycle
Cell nucleus
Cytoplasm
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Lung, neoplasm
Mammary gland, neoplasm
Ovary, neoplasm
Sarcoma
Signal transduction, biological
(predictive markers in cancer therapy)
IT Epidermal growth factor receptors
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(predictive markers in cancer therapy)
IT Kidney, neoplasm
(renal cell carcinoma; predictive markers in cancer therapy)
IT Carcinoma
(renal cell; predictive markers in cancer therapy)
IT Neoplasm
(solid, EGFR-expressing; predictive markers in cancer therapy)
IT 137632-07-6, Protein kinase ERK1 137632-08-7, Protein kinase ERK2
148640-14-6, Protein kinase AKT
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(predictive markers in cancer therapy)
IT 231277-92-2, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(predictive markers in cancer therapy)
IT 180288-69-1, Herceptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(predictive markers in cancer therapy)

L57 ANSWER 16 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:971922 HCAPLUS Full-text
DOCUMENT NUMBER: 140:23220
TITLE: Preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR
INVENTOR(S): Suzuki, Tsuyoshi; Kitano, Yasunori; Yano, Shinji
PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101491	A1	20031211	WO 2003-JP6988	20030603 ←

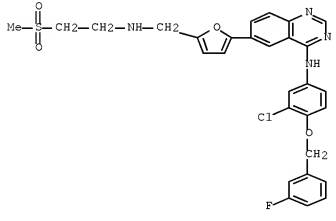
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003241898 A1 20031219 AU 2003-241898 20030603 ←
EP 1510221 A1 20050302 EP 2003-733264 20030603 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2005148607 A1 20050707 US 2005-516360 20050304 ←
PRIORITY APPLN. INFO.: JP 2002-162130 A 20020603 ←
WO 2003-JP6988 W 20030603 ←

OTHER SOURCE(S): MARPAT 140:23220
ED Entered STN: 14 Dec 2003
AB Her2 and/or EGFR inhibitors to be administered to subjects with the overexpression or activation of Her2 and/or EGFR that have been subjected to an examination for detecting the expression or activity of Her2 and/or EGFR and thus regarded as having the overexpression or activation of Her and/or EGFR; and medicinal compns. Containing such an inhibitor.
IT 231277-92-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K045-00
ICS A61K031-517; A61K031-519; A61K031-5377; A61P009-10; A61P017-06; A61P027-02; A61P035-00
CC 1-6 (Pharmacology)
IT Uterus, neoplasm
(cervix; quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)
IT Intestine, neoplasm

(colon; quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)

IT Neoplasm
(metastasis, angiogenesis associated with; quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)

IT Angiogenesis inhibitors
Angiogenesis inhibitors
Antitumor agents
Arteriosclerosis
Human
Lung, neoplasm
Pancreas, neoplasm
Psoriasis
(quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)

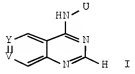
IT 231277-79-5 231277-81-9 231277-84-2 231277-88-6 231277-89-7
231277-90-0 231277-91-1 231277-92-2 231277-98-8
231278-00-5 231278-02-7 231278-05-0 267243-28-7 314771-08-9
386744-56-5 633370-23-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 17 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:836903 HCAPLUS Full-text
DOCUMENT NUMBER: 139:317433
TITLE: Cancer treatment method comprising administering an erb-family inhibitor and a raf and/or ras inhibitor
INVENTOR(S): Spector, Neil Lee; Xia, Wenle
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086467	A1	20031023	WO 2003-US10747	20030408 ←
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003221684	A1	20031027	AU 2003-221684	20030408 ←
EP 1492568	A1	20050105	EP 2003-718262	20030408 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005534623	T	20051117	JP 2003-583483	20030408 ←

US 2005176740 A1 20050811 US 2004-510542 20041007 ←
PRIORITY APPLN. INFO.: US 2002-370807P P 20020408 ←
WO 2003-US10747 W 20030408 ←
OTHER SOURCE(S): MARPAT 139:317433
ED Entered STN: 24 Oct 2003
GI

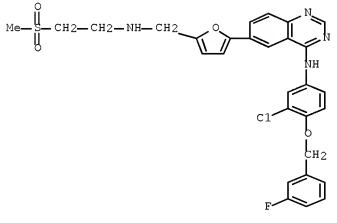


AB The invention provides a method for treating cancer in a mammal, as well as pharmaceutical combinations useful in such treatment. In particular, the method relates to a cancer treatment method that includes administering an erb family inhibitor and a Raf and/or ras inhibitor to a mammal suffering from a cancer. Preparation of compds., e.g. erbB-2/EGFR inhibitor I, is described.

IT 231277-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K045-06
ICS A61K031-517; A61K031-519; A61P035-00

CC 1-6 (Pharmacology)
Section cross-reference(s): 28

ST erb raf ras inhibitor combination cancer treatment; furyl quinazolinamine _acque prepn erbB2 EGFR inhibitor antitumor combination

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Ha-(Val.12)-ras; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Raf, bRaf-1; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Raf, bRaf; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Raf, cRaf-1; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Raf; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Pancreas, neoplasm
(duct cell adenocarcinoma; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(erb family; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Antitumor agents
Apoptosis
Drug interactions
Neoplasm
Pancreas, neoplasm
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Epidermal growth factor receptors
Ras proteins
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Carcinoma
(pancreatic ductal adenocarcinoma; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT Phosphorylation, biological
(protein; erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT 137632-07-6, Erk1 kinase 137632-08-7, Erk2 kinase 137632-09-8, ErbB-2 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT 405554-52-1P 502638-69-9P 614753-57-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
IT 202272-68-2P 220904-82-5P 231277-92-2P 319917-44-7P
319917-46-9P 320337-12-0P 405554-53-2P 405554-55-4P 502638-70-2P
502638-71-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

IT 614753-58-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

IT 107-14-2, Chloroacetonitrile 124-40-3, Dimethylamine, reactions 593-56-6, Methoxylamine hydrochloride 872-85-5, Pyridine-4-carbaldehyde 3680-02-2, Methyl vinyl sulfone 7664-93-9, Sulfuric acid, reactions 7803-49-8, Hydroxylamine, reactions 10312-83-1, Methoxyacetaldehyde 15182-92-0 26934-35-0 34598-49-7, 5-Bromoindanone 43018-72-0, (4-Chlorophenoxy)acetaldehyde 49773-20-8 59020-10-9 160809-34-7 193354-13-1, 5-Iodooxindole 202272-67-1 231278-84-5 319917-43-6 320337-48-2 614753-55-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

IT 220904-98-3P 405554-62-3P 405554-63-4P 405554-64-5P 405554-66-7P 405554-85-0P 502639-21-6P 502639-22-7P 502639-23-8P 502639-24-9P 502639-25-0P 614753-56-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

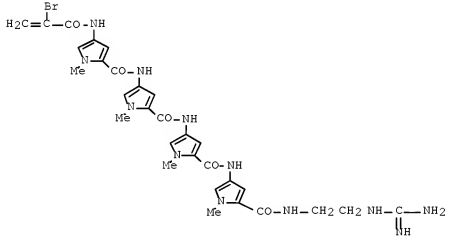
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 18 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:532545 HCAPLUS Full-text
DOCUMENT NUMBER: 139:95455
TITLE: Combined therapy against tumors comprising substituted acryloyl distamycin derivatives and protein kinase (serine/threonine kinase) inhibitors
INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo
PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003055522	A1	20030710	WO 2002-EP13092	20021218 ←
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472008	A1	20030710	CA 2002-2472008	20021218 ←

AU 2002352090	A1	20030715	AU 2002-352090	20021218	←
EP 1461083	A1	20040929	EP 2002-787763	20021218	←
EP 1461083	B1	20060329			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002015454	A	20041123	BR 2002-15454	20021218	←
HU 2004002639	A2	20050428	HU 2004-2639	20021218	←
CN 1617744	A	20050518	CN 2002-827674	20021218	←
JP 2005516025	T	20050602	JP 2003-556098	20021218	←
AT 321572	T	20060415	AT 2002-787763	20021218	←
PT 1461083	T	20060831	PT 2002-787763	20021218	←
ES 2263835	T3	20061216	ES 2002-2787763	20021218	←
NZ 533854	A	20070531	NZ 2002-533854	20021218	←
MX 2004PA06543	A	20041004	MX 2004-PA6543	20040702	←
ZA 2004005290	A	20050617	ZA 2004-5290	20040702	←
NO 2004003217	A	20040730	NO 2004-3217	20040729	←
US 2006084612	A1	20060420	US 2005-500606	20050505	←
IN 2007DN00991	A	20070803	IN 2007-DN991	20070206	←
PRIORITY APPLN. INFO.:			EP 2002-75052 A	20020102	←
			WO 2002-EP13092 W	20021218	←
			IN 2004-DN1960 A3	20040708	

OTHER SOURCE(S): MARPAT 139:95455
ED Entered STN: 11 Jul 2003
GI



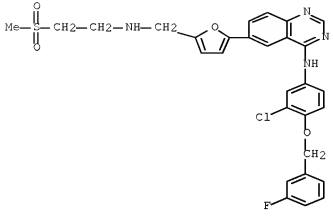
AB The present invention provides the combined use of acryloyl distamycin _acques., in particular α-bromo- and α-chloro-acryloyl distamycin _acques., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

IT 231277-92-2, GW572016
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combined antitumor therapy comprising acryloyl distamycin _acques. And protein kinase (serine/threonine kinase) inhibitors)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K045-06
ICS A61K031-40; A61K031-415; A61P035-00

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

IT Angiogenesis inhibitors
Antitumor agents
(combined antitumor therapy comprising acryloyl distamycin _acques. And protein kinase (serine/threonine kinase) inhibitors)

IT 9026-43-1, Serine/threonine kinase 15639-50-6, Safingol 112953-11-4, UCN-01 120685-11-2, CGP 41251 132244-47-4 132268-27-0 146426-40-6, Flavopiridol 157716-52-4, Perifosine 177409-55-1 177409-56-2 183319-69-9, OSI-774 183488-70-2, CEP 2563 184475-35-2, ZD-1839 187724-61-4, PKI 166 203258-38-2 204005-46-9, SU 5416 212141-54-3, CGP 79787 220127-57-1, STI571 231277-92-2, GW572016 245045-61-8 257933-82-7, EKB-569 342797-98-2 342798-29-2 383363-69-7 383363-70-0 443913-73-3, ZD 6474 557795-02-5, CP 564959 557795-03-6, ZD 2171 557795-19-4 557795-21-8, CI 202
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined antitumor therapy comprising acryloyl distamycin _acques. And protein kinase (serine/threonine kinase) inhibitors)

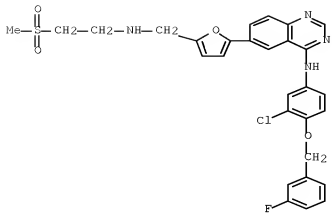
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 19 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:607455 HCAPLUS Full-text
DOCUMENT NUMBER: 139:159940
TITLE: Use of tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions
INVENTOR(S): Jung, Birgit; Puschner, Hubert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10204462	A1	20030807	DE 2002-10204462	20020205 ←
CA 2472293	A1	20030814	CA 2003-2472293	20030128 ←
WO 2003066060	A2	20030814	WO 2003-EP814	20030128 ←
WO 2003066060	A3	20040115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003206785	A1	20030902	AU 2003-206785	20030128 ←
EP 1474149	A2	20041110	EP 2003-704477	20030128 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005525328	T	20050825	JP 2003-565484	20030128 ←
US 2003149062	A1	20030807	US 2003-353616	20030129 ←
PRIORITY APPLN. INFO.:			DE 2002-10204462 A	20020205 ←
			WO 2003-EP814 W	20030128 ←

OTHER SOURCE(S): MARPAT 139:159940
ED Entered STN: 08 Aug 2003
AB The invention discloses the use of quinazoline _acques. (Markush included), or the compds. (1) 4-[(3-chloro-4-fluorphenyl)amino]-6-[(4-dimethylaminocyclohexyl)amino]pyrimido[5,4-d]pyrimidine; (2) 4-[©-(1-phenylethyl)amino]-6-(4-hydroxyphenyl)-7H-pyrrolo[2,3- d]pyrimidine; (3) 4-[(3-Chloro-4-(3-fluoro-4-benzyloxy)phenyl)amino]-6-[5- (((2-methansulfonylethyl)amino)methyl)-furan-2-yl]quinazoline; or the antibody cetuximab C225, trastuzumab, ABX-EGF, Mab ICR-62 and EGFR antisense, their tautomers, their stereoisomers and their salts, in particular their physiol. Compatible salts with inorg. Or organic acids or bases, for the production of a medication for prevention or treatment of diseases of the respiratory system or the lung. Preparation of quinazoline compds. Is included.
IT 231277-92-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K031-519
ICS A61K031-517
CC 1-9 (Pharmacology)
Section cross-reference(s): 28
IT Digestive tract, neoplasm
(polyposis; tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)
IT 253-82-7D, Quinazoline, _acques. 180288-69-1, Trastuzumab 183321-74-6
184475-35-2 187724-61-4 196612-94-9 205923-56-4, Cetuximab
231277-92-2 267243-28-7 290302-19-1 314771-10-3
314771-31-8 339177-26-3, ABX-EGF 402496-85-9 402569-98-6
402570-00-7 402724-17-8 402855-53-2 573649-60-2 573649-61-3
573649-62-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)

L57 ANSWER 20 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:917646 HCAPLUS Full-text
DOCUMENT NUMBER: 140:38051
TITLE: Epidermal Growth Factor Receptor Autocrine Signaling in RIE-1 Cells Transformed by the Ras Oncogene Enhances Radiation Resistance
AUTHOR(S): Grana, Theresa M.; Sartor, Carolyn I.; Cox, Adrienne D.
CORPORATE SOURCE: Curriculum in Genetics and Molecular Biology, Department of Radiation Oncology, University of North Carolina, Chapel Hill, NC, USA
SOURCE: Cancer Research (2003), 63(22), 7807-7814
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Nov 2003
AB Oncogenic forms of the small GTPase Ras increase the resistance of cells to killing by ionizing radiation (IR). Although not all of the signaling pathways for radioresistance are well defined, it is now clear that Ras-dependent signaling pathways involved in radioresistance include those mediated by phosphatidylinositol 3'-kinase (PI3-K) and Raf. Nevertheless, PI3-K and Raf together are not sufficient to reconstitute all of the

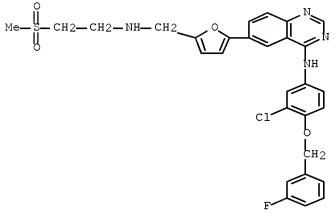
resistance conferred by Ras, indicating that other effectors must also contribute. We show here that Ras-driven autocrine signaling through the epidermal growth factor receptor (EGFR) also contributes to radioresistance in Ras-transformed cells. Conditioned media (CM) collected from RIE-1 rat intestinal epithelial cells expressing oncogenic Ras increased the survival of irradiated cells. Ras-CM contains elevated levels of the EGFR ligand transforming growth factor α (TGF-α). Both Ras-CM and TGF-α stimulated EGFR phosphorylation, and exogenous TGF-α mimicked the effects of Ras-CM to increase radioresistance. Blocking EGFR signaling with the EGFR/HER-2 kinase inhibitor (KI) GW572016 decreased the postradiation survival of irradiated Ras-transformed cells and normal cells but had no effect on the survival of unirradiated cells. Ras-CM and TGF-α also increase PI3-K activity downstream of the EGFR and increase postradiation survival, both of which are abrogated by GW572016. Thus, Ras utilizes autocrine signaling through EGFR to increase radioresistance, and the EGFR KI GW572016 acts as a radiosensitizer. The observation that Ras-transformed cells can be sensitized to killing by ionizing radiation with GW572016 demonstrates that EGFR Kis could potentially be used to radiosensitize tumors in which radioresistance is dependent on Ras-driven autocrine signaling through EGFR.

IT 231277-92-2, GW572016

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 2, 14

ST EGF receptor Ras signaling radioresistance tumor GW572016

IT Signal transduction, biological
Transformation, neoplastic
(Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)

IT Intestine, neoplasm
(carcinoma; Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)

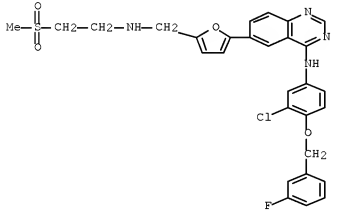
IT Carcinoma
Epithelium
(intestinal; Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)
IT 231277-92-2, GW572016
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 21 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:555376 HCAPLUS Full-text
DOCUMENT NUMBER: 137:119644
TITLE: 4-Quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation.
INVENTOR(S): Lackey, Karen Elizabeth; Spector, Neil; Wood, Edgar Raymond, III; Xia, Wenle
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002056912	A2	20020725	WO 2002-US1130	20020114 ←
WO 2002056912	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002236765	A1	20020730	AU 2002-236765	20020114 ←
EP 1353693	A2	20031022	EP 2002-703127	20020114 ←
EP 1353693	B1	20050316		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004523522	T	20040805	JP 2002-557419	20020114 ←
EP 1488809	A1	20041222	EP 2004-77577	20020114 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
EP 1512413	A2	20050309	EP 2004-78283	20020114 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
AT 290882	T	20050415	AT 2002-703127	20020114 ←
ES 2236481	T3	20050716	ES 2002-2703127	20020114 ←
US 2004053946	A1	20040318	US 2003-466290	20030715 ←
US 7141576	B2	20061128		

US 2007148261 A1 20070628 US 2006-548413 20061011 ←
PRIORITY APPLN. INFO.: US 2001-262402P P 20010116 ←
EP 2002-703127 A3 20020114 ←
WO 2002-US1130 W 20020114 ←
US 2003-466290 A1 20030715 ←

OTHER SOURCE(S): MARPAT 137:119644
ED Entered STN: 26 Jul 2002
AB A method of treating cancer is described which includes administration of a 4-quinazolineamine (preparation included) and at least one other antineoplastic agent. Also described is a pharmaceutical combination including the 4-quinazolineamines.
IT 231277-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
RN 231277-92-2 HCAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM A61K045-06
ICS A61K031-505; A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 28, 63
ST quinazolineamine _acque prepn antitumor combination pharmaceutical
IT Hormones, animal, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and hormone analogs; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT Microtubule
(anti-microtubule agents; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT Nutrients
(antinutrients; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT Cell cycle

(cell cycle signaling inhibitors; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Neoplasm
Neoplasm
(head and neck; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Signal transduction, biological
(inhibitors; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Apoptosis
(pro-apoptotic agents; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Alkylating agents, biological
Angiogenesis inhibitors
Antibiotics
Antitumor agents
Drug delivery systems
Head and Neck, neoplasm
Head and Neck, neoplasm
Human
Immunotherapy
Lung, neoplasm
Mammary gland, neoplasm
Neoplasm
(quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Diterpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ras, inhibitors; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT 101463-26-7, Platelet-derived growth factor receptor tyrosine kinase 103843-29-4, Gene IGFR1 tyrosine kinase 108891-60-7 115926-52-8, PI3 kinase 131384-38-8, Farnesyltransferase 135371-29-8, Geranylgeranyl protein transferase 139691-76-2, Raf kinase 141349-86-2, CDK2 kinase 141349-89-5, Src kinase 142805-56-9, Topoisomerase II 143180-75-0 144697-17-6, c-Src kinase 147014-97-9, CDK4 kinase 147302-47-4, TrkC protein tyrosine kinase 148047-29-4, TIE2 receptor kinase 148640-14-6, Akt kinase 149146-91-8, TrkB tyrosine kinase 149147-12-6, BTK kinase 150977-45-0, VEGF receptor tyrosine kinase 2 152787-58-1, TrkA receptor tyrosine kinase 303014-92-8, CDK6 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

IT 5847-59-6P, 2-Bromo-4-nitrophenol 202197-26-0P 231278-20-9P 231278-84-5P 320337-13-1P 320337-14-2P 320337-18-6P 320337-22-2P 320337-27-7P 443882-99-3P 443883-07-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; quinazolineamine derivative combination with

other
antineoplastic agent for cancer treatment, and compound preparation)
IT 231277-92-2P 388082-75-5P 388082-77-7P 388082-78-8P
388082-82-4P 443883-05-4P 443883-12-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT 7440-06-4D, Platinum, coordination complexes 33069-62-4, Paclitaxel 41575-94-4, Carboplatin 71486-22-1, Vinorelbine 388082-79-9 388082-81-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT 202197-78-2P, 4-Chloro-7-iodoquinazoline
RL: SPN (Synthetic preparation); PREP (Preparation)
(quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT 104-15-4, p-Toluenesulfonic acid, reactions 456-41-7, 3-Fluorobenzyl bromide 456-47-3, 3-Fluorobenzyl alcohol 619-08-9, 2-Chloro-4-nitrophenol 5197-28-4, 2-Bromo-4-nitroanisole 49773-20-8 97674-02-7 98556-31-1, 4-Chloro-6-iodoquinazoline 118505-28-5 202197-77-1, 7-Iodoquinazolin-4-one 231278-74-3 388082-76-6 443883-09-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)
IT 141436-78-4, Protein kinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(zeta, inhibitors; quinazolineamine derivative combination with other antineoplastic agent for cancer treatment, and compound preparation)

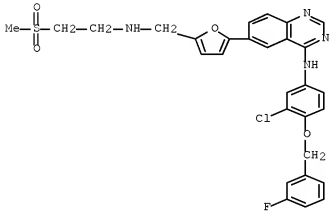
L57 ANSWER 22 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:668812 HCAPLUS Full-text
DOCUMENT NUMBER: 138:280796
TITLE: Anti-tumor activity of GW572016: a dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways
AUTHOR(S): Xia, Wenle; Mullin, Robert J.; Keith, Barry R.; Liu, Lei-Hua; Ma, Hong; Rusnak, David W.; Owens, Gary; Alligood, Krystal J.; Spector, Neil L.
CORPORATE SOURCE: GlaxoSmithKline, Department of Discovery Medicine, Research Triangle Park, North Carolina, NC, 27709-3398, USA
SOURCE: Oncogene (2002), 21(41), 6255-6263
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Sep 2002
AB Dual EGFR/erbB2 inhibition is an attractive therapeutic strategy for epithelial tumors, as ligand-induced erbB2/EGFR heterodimerization triggers potent proliferative and survival signals. Here we show that a small mol., GW572016, potently inhibits both EGFR and erbB2 tyrosine kinases leading to growth arrest and/or apoptosis in EGFR and erbB2-dependent tumor cell lines. GW572016 markedly reduced tyrosine phosphorylation of EGFR and erbB2, and inhibited activation of Erk1/2 and AKT, downstream effectors of proliferation and cell survival, resp. Complete inhibition of activated AKT in erbB2

overexpressing cells correlated with a 23-fold increase in apoptosis compared with vehicle controls. EGF, often elevated in cancer patients, did not reverse the inhibitory effects of GW572016. These observations were reproduced in vivo, where GW572016 treatment inhibited activation of EGFR, erbB2, Erk1/2 and AKT in human tumor xenografts. Erk1/2 and AKT represent potential biomarkers to assess the clin. Activity of GW572016. Inhibition of activated AKT in EGFR or erbB2-dependent tumors by GW572016 may lead to tumor regressions when used as a monotherapy, or may enhance the anti-tumor activity of chemotherapeutics, since constitutive activation of AKT has been linked to chemo-resistance.

IT 231277-92-2, GW 572016
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



CC 1-6 (Pharmacology)

IT Antitumor agents
Apoptosis
Human
(GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)

IT Carcinoma
Carcinoma
(head and neck squamous cell carcinoma; GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)

IT Head and Neck, neoplasm
Head and Neck, neoplasm
(squamous cell carcinoma; GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)

IT 231277-92-2, GW 572016
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 23 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:50639 HCAPLUS Full-text
DOCUMENT NUMBER: 134:100886
TITLE: Preparation of anilinoquinazolines as protein tyrosine kinase inhibitors
INVENTOR(S): Cockerill, George Stuart; Lackey, Karen Elizabeth
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004111	A1	20010118	WO 2000-US18128	20000630 ←
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1192151	A1	20020403	EP 2000-943348	20000630 ←
EP 1192151	B1	20071107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
JP 2003504363	T	20030204	JP 2001-509721	20000630 ←
AT 377597	T	20071115	AT 2000-943348	20000630 ←
US 6933299	B1	20050823	US 2002-30527	20020109 ←
US 2005143401	A1	20050630	US 2005-61578	20050218 ←
US 7084147	B2	20060801		
US 2006189637	A1	20060824	US 2006-400284	20060407 ←
US 7189734	B2	20070313		
US 2007093512	A1	20070426	US 2006-562047	20061121 ←
US 7265123	B2	20070904		
US 2008004294	A1	20080103	US 2007-832187	20070801 ←

PRIORITY APPLN. INFO.:	GB 1999-16213	A	19990709 ←
	GB 1999-16218	A	19990709 ←
	WO 2000-US18128	W	20000630 ←
	US 2002-30527	A3	20020109 ←
	US 2005-61578	A3	20050218
	US 2006-400284	A3	20060407
	US 2006-562047	A3	20061121

OTHER SOURCE(S): MARPAT 134:100886
ED Entered STN: 19 Jan 2001
GI

(13) STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

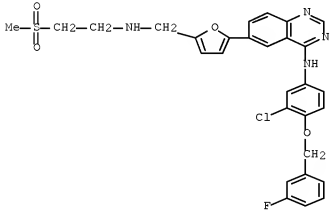
AB The title compds. [I; X = CR1 and Y = N; or X = N and Y = CR1; X = CR1 and Y = CR2; X = CR2 and Y = CR1; R1 = Ar(CH2)Pzch2CH2SO2R5 (wherein Ar = (un)substituted Ph, furan, thiophene, etc.; Z = O, S, NH, NR6; p = 1-4; R5 = alkyl substituted by 5-10 membered heterocyclic group, 3-10 membered carbocyclic group, etc.; R6 = alkyl, alkoxyalkyl, hydroxyalkyl, etc.); R2 = H, halo, OH, etc.; R3 = pyridylmethoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy; R4 = H, halo, alkyl, etc.; with the proviso that when p = 1 and Z = NH, R5 cannot represent Me] which exhibit protein tyrosine kinase inhibition, in particular erbB family kinase inhibition, and useful in treating cancer and psoriasis, were prepared E.g., a multi-step synthesis of the anilinoquinazoline II was given. Biol. Data (erbB-2, erbB-4, EGFr, and cell proliferation inhibition) for the compds. I were presented.

IT 231277-92-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM C07D405-04
ICS C07D405-14; C07D471-04; C07D417-04; A61K031-505; A61P035-00; A61P011-00; A61P019-02; A61P017-06; C07D471-04; C07D213-00; C07D233-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT Antitumor agents
Psoriasis
(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)

IT 100-39-0, Benzyl bromide 100-51-6, Benzyl alcohol, reactions 106-94-5, 1-Bromopropane 446-32-2, 2-Amino-4-fluorobenzoic acid 456-47-3, 3-Fluorobenzyl alcohol 867-13-0, Triethylphosphonoacetate 1461-22-9, Tributyltin chloride 3680-02-2, Methyl vinyl sulfone 5197-28-4, 2-Bromo-4-nitroanisole 5198-80-1, 2-Bromothiazole-4-carbaldehyde 5326-23-8, 6-Chloronicotinic acid 5535-48-8, Phenyl vinyl sulfone 6373-46-2, 4-Benzyloxyaniline 7605-28-9, Phenylsulfonylacetonitrile 18542-42-2 38267-96-8, 4-Chloro-6-bromoquinazoline 49773-20-8 51388-20-6, 4-Benzyloxyaniline hydrochloride 90004-09-4, 7-Aminoquinazolin-4-one 97674-02-7, Tributyl(1-ethoxyvinyl)stannane 98556-31-1, 4-Chloro-6-iodoquinazoline 118505-28-5 120069-21-8 130493-24-2, 5-(Tributylstannyl)-furan-3-carbaldehyde 175137-61-8

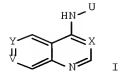
179248-66-9 202198-16-1 231277-92-2 231278-14-1
231278-64-1, 4-Chloro-6-iodo-7-fluoroquinazoline 231278-68-5
320337-46-0 320337-47-1 320337-48-2 320337-49-3 320337-50-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 24 OF 51 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:451297 HCAPLUS Full-text
DOCUMENT NUMBER: 131:102288
TITLE: Bicyclic heteroaromatic compounds [quinazolinamines, pyridopyrimidines, and analogs] useful as protein tyrosine kinase inhibitors
INVENTOR(S): Carter, Malcolm Clive; Cockerill, George Stuart; Guntrip, Stephen Barry; Lackey, Karen Elizabeth; Smith, Kathryn Jane
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

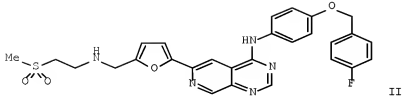
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9935146	A1	19990715	WO 1999-EP48	19990108 ←
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2317589	A1	19990715	CA 1999-2317589	19990108 ←
CA 2317589	C	20070807		
AU 9922783	A	19990726	AU 1999-22783	19990108 ←
AU 749549	B2	20020627		
BR 9906904	A	20001017	BR 1999-6904	19990108 ←
EP 1047694	A1	20001102	EP 1999-902522	19990108 ←
EP 1047694	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002015	T2	20010122	TR 2000-2015	19990108 ←
HU 2001000941	A2	20010928	HU 2001-941	19990108 ←
EE 200000411	A	20011217	EE 2000-411	19990108 ←
EE 4616	B1	20060417		
JP 2002500225	T	20020108	JP 2000-527545	19990108 ←
JP 3390741	B2	20030331		
JP 2002326990	A	20021115	JP 2002-92102	19990108 ←
NZ 505456	A	20030630	NZ 1999-505456	19990108 ←
CN 1134437	B	20040114	CN 1999-803887	19990108 ←
AT 270670	T	20040715	AT 1999-902522	19990108 ←
EP 1454907	A1	20040908	EP 2004-76762	19990108 ←
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1460072	A1	20040922	EP 2004-76761	19990108 ←

EP 1460072	B1	20060405				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL						
PT 1047694	T	20041130	PT 1999-902522		19990108	←
ES 2221354	T3	20041216	ES 1999-902522		19990108	←
AP 1446	A	20050930	AP 2000-1861		19990108	←
W: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW						
AT 322491	T	20060415	AT 2004-76761		19990108	←
PT 1460072	T	20060731	PT 2004-76761		19990108	←
ES 2262087	T3	20061116	ES 2004-76761		19990108	←
PL 192746	B1	20061229	PL 1999-341595		19990108	←
SK 285405	B6	20070104	SK 2000-1050		19990108	←
CZ 298047	B6	20070606	CZ 2000-2587		19990108	←
ZA 9900172	A	20000711	ZA 1999-172		19990111	←
TW 477788	B	20020301	TW 1999-88100388		19990112	←
US 6727256	B1	20040427	US 2000-582746		20000630	←
NO 2000003561	A	20000911	NO 2000-3561		20000711	←
NO 316176	B1	20031222				
MX 2000PA06824	A	20010405	MX 2000-PA6824		20000711	←
HR 2000000469	A1	20010630	HR 2000-469		20000712	←
HR 2000000469	B1	20070531				
IN 2000KN00130	A	20050311	IN 2000-KN130		20000712	←
BG 104668	A	20010430	BG 2000-104668		20000807	←
BG 64825	B1	20060531				
HK 1031883	A1	20050304	HK 2001-102589		20010411	←
US 2002147205	A1	20021010	US 2002-71358		20020208	←
US 6713485	B2	20040330				
US 2003176451	A1	20030918	US 2003-342810		20030115	←
US 2005130996	A1	20050616	US 2005-50033		20050203	←
US 7109333	B2	20060919				
US 2007015775	A1	20070118	US 2006-532926		20060919	←
US 2007238875	A1	20071011	US 2007-752582		20070523	←
PRIORITY APPLN. INFO.:			GB 1998-569	A	19980112	←
			EP 1999-902522	A3	19990108	←
			JP 2000-527545	A3	19990108	←
			WO 1999-EP48	W	19990108	←
			US 2000-582746	A1	20000630	←
			US 2003-342810	A1	20030115	←
			US 2005-50033	A1	20050203	

OTHER SOURCE(S): MARPAT 131:102288
ED Entered STN: 23 Jul 1999
GI



I



II

AB Title compds. I and their salts and solvates are disclosed [wherein X = N or CH; Y = CR1 and V = N; or Y = N and V = CR1; or Y = CR1 and V = CR2; or Y = CR2 and V = CR1; R1 = MeSO2CH2CH2NHCH2-Ar-, wherein Ar = (un)substituted Ph, furan, thiophene, pyrrole, or thiazole; R2 = H, halo, OH, C1-4 alkyl, C1-4 alkoxy, C1-4 alkylamino, or di[C1-4 alkyl]amino; U = Ph, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by R3 and optionally by R4; R3 = (halo)benzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and (halo)benzyloxy, PhSO2, (trihalomethyl)benzyl, (trihalomethyl)benzyloxy, (R5)n-substituted phthalimido; R4 = OH, halo, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, C1-4 alkoxy, (di)(alkyl)amino, C1-4 alkylthio, etc.; R5 = halo, C1-4 alkyl, C1-4 alkoxy; n = 0-3]. Also disclosed are methods for their preparation, pharmaceutical compns. Containing them, and their use in medicine. The compds. Are inhibitors of protein tyrosine kinases, and as such are useful in the treatment of cancer, psoriasis, and rheumatoid arthritis. Over 40 title compds. And numerous intermediates were prepared For example, 4,6-dichloropyrido[3,4-d]pyrimidine was condensed with 4-[(4-fluorobenzyl)oxy]aniline at the 4-chloro position, followed by Pd-catalyzed coupling with 5-(1,3-dioxolan-2-yl)-2-(tributylstannyl)furan at the 6-chloro position, hydrolysis of the dioxolane protecting group to give an aldehyde, reductive amination of the latter with MeSCH2CH2NH2, and finally S-oxidation with Oxone and acidification, to give title salt II.2HCl. In a methylene blue growth inhibition assay against 5 tumor cell lines, II.2HCl had an IC50 of < 5 μM against 4 of them, and an IC50 of 25-50 μM against the 5th.

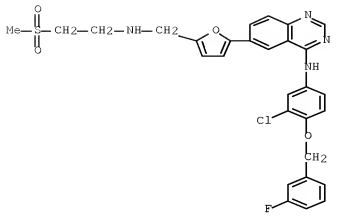
IT 231277-92-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of quinazolinamines and analogs as protein tyrosine kinase inhibitors)

RN 231277-92-2 HCAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (CA INDEX NAME)



IC ICM C07D471-04
ICS A61K031-505; A61K031-47; C07D405-04; C07D417-04; C07D405-14; C07D417-14; C07D471-04; C07D239-00; C07D221-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7
ST quinazolinamine prepn protein tyrosine kinase inhibitor antitumor; pyridopyrimidine quinazolinamine prepn treatment cancer psoriasis rheumatoid arthritis
IT Antiarthritics
Antitumor agents
(preparation of quinazolinamines and analogs as protein tyrosine kinase inhibitors)
IT 231277-64-8P 231277-65-9P 231277-66-0P 231277-67-1P 231277-69-3P
231277-70-6P 231277-71-7P 231277-72-8P 231277-73-9P 231277-74-0P
231277-75-1P 231277-76-2P 231277-77-3P 231277-78-4P 231277-79-5P
231277-80-8P 231277-81-9P 231277-82-0P 231277-83-1P 231277-84-2P
231277-85-3P 231277-86-4P 231277-87-5P 231277-88-6P 231277-89-7P
231277-90-0P 231277-91-1P 231277-92-2P 231277-93-3P
231277-94-4P 231277-95-5P 231277-96-6P 231277-97-7P 231277-98-8P
231277-99-9P 231278-00-5P 231278-01-6P 231278-02-7P 231278-03-8P
231278-04-9P 231278-06-1P 231278-07-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of quinazolinamines and analogs as protein tyrosine kinase inhibitors)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 25 OF 51 BIOSIS COPYRIGHT © 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:258630 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300258630
TITLE: Effect of GW572016 on ERBB-2 signaling, cell growth, and apoptosis in rat biliary cancer cells.
AUTHOR(S): Lai, Guan-Hua [Reprint Author]; Sirica, Alphonse E.
CORPORATE SOURCE: Pathology, Virginia Commonwealth University, 1101 East Marshall Street, Richmond, VA, 23298-0297, USA
ghlai@hsc.vcu.edu; asirica@hsc.vcu.edu
SOURCE: FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No. 163.10. http://www.fasebj.org/. e-file.

Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jun 2003
Last Updated on STN: 1 Aug 2003

AB Overexpression of ErbB-2 has been linked to cholangiocarcinogenesis in both experimental rodents and in the human. We have now investigated the effects of GW572016 (GlaxoSmithKline), a potent new small molecule inhibitor of epidermal growth factor receptor (ErbB-1) and of ErbB-2 tyrosine kinase activity, for its ability to suppress growth and induce apoptosis in a novel rat biliary cancer cell line (C611B ChC) constitutively overexpressing activated ErbB-2. ErbB1 was only weakly expressed in C611B ChC cells and they did not express ErbB-4. ErbB-3 was detected by Western Blotting in C611B ChC cells , but at a lower amount than ErbB-2,and evidence was obtained for ErbB-2/ErbB-3 heterodimer formation in these cells. GW572016 produced significant dose-dependent suppression of cell growth and induced prominent apoptosis in cultured C611B ChC cells. These effects correlated with a selective suppression of ErbB-2 tyrosine phosphorylation, and downstream, with inhibition of both the Akt and ERK ½ signaling pathways. Apoptosis induced by GW572016 in cultured C611B ChC cells involved actitivation of caspase-3 and associated cleavage of polyADP-ribose polymerase. These data strongly suggest GW572016 targeting of ErbB-2 overexpressed in biliary cancer cells may provide a novel therapeutic strategy for the treatment of a cancer for which there is currently no effective therapy.

CC General biology - Symposia, transactions and proceedings 00520
Cytology - General 02502
Cytology - Animal 02506
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Digestive system - Physiology and biochemistry 14004
Digestive system - Pathology 14006
Endocrine - General 17002
Neoplasms - Pathology, clinical aspects and systemic effects 24004

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Digestive System (Ingestion and Assimilation); Tumor Biology

IT Parts, Structures, & Systems of Organisms
biliary cancer cells

IT Diseases
biliary cancer: digestive system disease, neoplastic disease
Biliary Tract Neoplasms (MeSH)

IT Chemicals & Biochemicals
ErbB-1: epidermal growth factor receptor; ErbB-2: epidermal growth factor receptor; ErbB-2 tyrosine kinase; GW572016; caspase-3

IT Miscellaneous Descriptors
ERBB-2 signaling; apoptosis; cell growth

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
C611B ChC cell line (cell line): rat biliary cancer cell line
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 137632-09-8 (ErbB-2 tyrosine kinase)
231277-92-2 (GW572016)
169592-56-7 (caspase-3)

L57 ANSWER 26 OF 51 EMBASE COPYRIGHT © 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003468349 EMBASE Full-text
TITLE: HER-2-Targeted Therapy: Lessons Learned and Future Directions.
AUTHOR: Nahta R.; Esteva F.J.
CORPORATE SOURCE: F.J. Esteva, Dept. of Breast Medical Oncology, Univ. TX M. D. Anderson Cancer Ctr., Unit 424, 1515 Holcombe Boulevard, Houston, TX 77030-4009, United States. festeva@mdanderson.org
SOURCE: Clinical Cancer Research, (1 Nov 2003) Vol. 9, No. 14, pp. 5078-5084.
Refs: 92
ISSN: 1078-0432 CODEN: CCREF4
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 016 Cancer
027 Biophysics, Bioengineering and Medical Instrumentation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jan 2004
Last Updated on STN: 5 Jan 2004

AB HER-2 is overexpressed in 20-25% of invasive breast cancers and is associated with an aggressive tumor phenotype and reduced survival rates. The HER-2 status of a tumor is the critical determinant of response to the HER-2-targeted antibody trastuzumab. Thus, accurate assessment of HER-2 expression levels is essential for identifying breast cancer patients who will benefit from HER-2-targeted therapy. Trastuzumab combined with chemotherapy increases response rates, time to progression, and survival. However, the majority of cancers that initially respond to trastuzumab begin to progress again within 1 year. This minireview describes HER-2 targeting strategies currently in use or in stages of development for the treatment of breast cancer.

CT Medical Descriptors:
*breast cancer: DT, drug therapy
cancer growth
cancer survival
clinical trial
controlled study
enzyme linked immunosorbent assay
fluorescence in situ hybridization
gene expression
gene targeting
human
meta analysis
*oncogene neu
phase 2 clinical trial
phase 3 clinical trial
polymerase chain reaction
priority journal
randomized controlled trial
short survey
Western blotting
CT Drug Descriptors:

anthracycline: CT, clinical trial
anthracycline: CB, drug combination
anthracycline: DT, drug therapy
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PO, oral drug administration
canertinib: PD, pharmacology
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: DT, drug therapy
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: DT, drug therapy
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
E1A protein: CT, clinical trial
E1A protein: DT, drug therapy
epidermal growth factor receptor antibody: CT, clinical trial
epidermal growth factor receptor antibody: DT, drug therapy
epirubicin: CT, clinical trial
epirubicin: CB, drug combination
epirubicin: DT, drug therapy
gefitinib: CT, clinical trial
gefitinib: CB, drug combination
gefitinib: DT, drug therapy
gemcitabine: CT, clinical trial
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
monoclonal antibody: CT, clinical trial
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
navelbine: CT, clinical trial
navelbine: CB, drug combination
navelbine: DT, drug therapy
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
pertuzumab: CT, clinical trial
pertuzumab: DT, drug therapy
pertuzumab: PD, pharmacology
temsirolimus: CT, clinical trial
temsirolimus: PD, pharmacology
tipifarnib: CB, drug combination
tipifarnib: PD, pharmacology
*trastuzumab: CT, clinical trial
*trastuzumab: CB, drug combination
*trastuzumab: DT, drug therapy
*trastuzumab: PD, pharmacology
unclassified drug
virus protein: CT, clinical trial
virus protein: DT, drug therapy

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carboplatin) 41575-94-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (docetaxel) 114977-28-5; (epirubicin) 56390-09-1, 56420-45-2; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (navelbine) 71486-22-1; (paclitaxel) 33069-62-4; (temsirolimus) 162635-04-3, 343261-52-9;

(tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1
CN (1) cci 779; (2) ci 1033; (3) gw 572016; (4) herceptin; (5) iressa; (6) pd 183805; (7) r 115777; (8) zarnestra; (9) zd 1839
CO (1) Wyeth Ayerst (United States); (2) Pfizer (United States); (3) Glaxo SmithKline (United States); (4) Genentech (United States); (5) Astra Zeneca (United States); (6) Pfizer (United States); (7) Janssen (United States); (8) Janssen (United States); (9) Astra Zeneca (United States); Chiron; pharmexa; Targeted Genetics
NP (1) HercepTest; (2) Pathway HER2
CO (1) Dako (United States) ; (2) Ventana (United States)

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ACCESSION NUMBER: 2004038583 EMBASE Full-text
TITLE: ErbB family targeting.
AUTHOR: Black J.D.; Brattain M.G.; Krishnamurthi S.A.; Dawson D.M.; Willson J.K.V.
CORPORATE SOURCE: M.G. Brattain, Dept. of Pharmacology/Therapeutics, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, United States. _acques.brattain@roswellpark.org
SOURCE: Current Opinion in Investigational Drugs, (Dec 2003) Vol. 4, No. 12, pp. 1451-1454.
Refs: 31
ISSN: 1472-4472 CODEN: CIDREE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004

AB Drugs for specific molecular targets have generated a great deal of excitement for their potential in cancer treatment, particularly with respect to our molecular understanding of cancer in recent years. The clinical utility of antibodies and small molecule kinase inhibitors has been demonstrated. The ErbB family of receptors is at the forefront of targets that are the subject of clinical trials. However, the activities of epidermal growth factor receptor antagonists have not been impressive as single agents. One of the lessons learned with this class of targets is that we currently do not know how to optimally apply them to the treatment of cancer. This review will discuss the issues contributing to this situation and the approaches that are currently being launched to resolve these issues. .COPYRGT. Current Drugs.

CT Medical Descriptors:
acne: SI, side effect
breast cancer: DT, drug therapy
breast cancer: ET, etiology
cancer: DT, drug therapy
cancer: ET, etiology
cancer classification
clinical trial
colon cancer: DT, drug therapy
colon cancer: ET, etiology
colon carcinoma: DT, drug therapy
drug eruption: SI, side effect
drug toxicity: SI, side effect
enzyme inhibition

human
molecular interaction
monotherapy
protein targeting
review
signal transduction
CT Drug Descriptors:
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
6 o alkylguanine DNA alkyltransferase: EC, endogenous compound
6 o benzylguanine: AE, adverse drug reaction
6 o benzylguanine: CT, clinical trial
6 o benzylguanine: DO, drug dose
6 o benzylguanine: IT, drug interaction
6 o benzylguanine: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: CM, drug comparison
antineoplastic agent: DO, drug dose
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
canertinib: AE, adverse drug reaction
canertinib: CM, drug comparison
canertinib: DO, drug dose
canertinib: PD, pharmacology
carmustine: IT, drug interaction
carmustine: PD, pharmacology
cetuximab: AE, adverse drug reaction
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
*epidermal growth factor receptor: EC, endogenous compound
epidermal growth factor receptor 2: EC, endogenous compound
epidermal growth factor receptor antagonist: AE, adverse drug reaction
epidermal growth factor receptor antagonist: DO, drug dose
epidermal growth factor receptor antagonist: DT, drug therapy
epidermal growth factor receptor antagonist: PD, pharmacology
lapatinib: CT, clinical trial
lapatinib: CM, drug comparison
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
somatomedin C receptor: EC, endogenous compound
unclassified drug
vandetanib: PD, pharmacology
RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (6 o benzylguanine) 19916-73-5; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carmustine) 154-93-8; (cetuximab) 205923-56-4; (epidermal growth factor receptor 2) 137632-09-8; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3
CN (1) ci 1033; (2) erbitux; (3) erbitux; (4) erbitux; (5) gw 2016; (6) imc c225; (7) imc c225; (8) imc c225; (9) su 6668; (10) zd 6474
CO (1) Pfizer; (2) Bristol Myers Squibb; (3) Imclone; (4) Merck AG; (5) Glaxo SmithKline; (6) Bristol Myers Squibb; (7) Imclone; (8) Merck AG; (9) Sugen; (10) Astra Zeneca

L57 ANSWER 28 OF 51 EMBASE COPYRIGHT © 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004173798 EMBASE Full-text
TITLE: Targeted drugs in oncology: New names, new

mechanisms, new paradigm.
AUTHOR: Rotea Jr. W.; Saad E.D.
CORPORATE SOURCE: Dr. W. Rotea Jr., R. Vigario Albernaz 785/64, 04134-021, Sao Paulo, Brazil. rotea@uol.com.br
SOURCE: American Journal of Health-System Pharmacy, (15 Jun 2003) Vol. 60, No. 12, pp. 1233-1245.
Refs: 121
ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 May 2004
Last Updated on STN: 13 May 2004

AB The molecular mechanisms of action, clinical development, and efficacy and safety of targeted antineoplastic drugs are discussed. Recently introduced mechanism-based systemic therapies for cancer may be more specific, less toxic, and more effective and represent a paradigm shift in treatment. Currently, receptor tyrosine kinases (RTKs), nonreceptor kinases, the angiogenic molecules, the enzymes involved in extracellular matrix degradation, and the enzymes responsible for protein anchorage to the cytoplasmic membrane are among the targets against which specific interventions have been developed. Monoclonal antibodies against the extracellular portion of RTKs and small-molecule inhibitors of their tyrosine kinase activity are strategies in more advanced phases of clinical development. Over the next few years, one can expect to see the results of many studies of such new pharmacologic agents or combinations. It seems likely, at this point, that targeted drugs will be used in association with existing medical, surgical, and radiotherapeutic modalities and will play an important role in the ultimate goal of reducing the burden of cancer. Targeting of molecular abnormalities that are differentially expressed in tumors may represent a more specific and less toxic way of treating cancer.

CT Medical Descriptors:
adult respiratory distress syndrome: SI, side effect
asthenia: SI, side effect
bacterial infection: SI, side effect
bone marrow toxicity: SI, side effect
chill: SI, side effect
clinical trial
congestive heart failure: SI, side effect
constipation: SI, side effect
drug efficacy
drug mechanism
drug safety
drug targeting
edema: SI, side effect
enzyme inhibition
fever: SI, side effect
headache: SI, side effect
human
hypotension: SI, side effect
muscle cramp: SI, side effect
musculoskeletal disease: SI, side effect
nausea: SI, side effect
neuropathy: SI, side effect
neutropenia: SI, side effect
*oncology

priority journal
rash: SI, side effect
review
side effect: SI, side effect
somnolence: SI, side effect
thrombocytopenia: SI, side effect
tumor lysis syndrome: SI, side effect
vein occlusion: SI, side effect
virus infection: SI, side effect
weight gain

CT Drug Descriptors:

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: CT, clinical trial
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: PD, pharmacology
alemtuzumab: PD, pharmacology
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: CB, drug combination
angiogenesis inhibitor: PD, pharmacology
anthracycline: CB, drug combination
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: PD, pharmacology
canertinib: CT, clinical trial
canertinib: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: PD, pharmacology
cisplatin: CB, drug combination
cyclophosphamide: CB, drug combination
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
doxorubicin: CB, drug combination
erlotinib: CT, clinical trial
erlotinib: CB, drug combination
erlotinib: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: PD, pharmacology
gemtuzumab ozogamicin: AE, adverse drug reaction
gemtuzumab ozogamicin: CT, clinical trial
gemtuzumab ozogamicin: CM, drug comparison
gemtuzumab ozogamicin: PD, pharmacology
ibritumomab tiuxetan: AE, adverse drug reaction
ibritumomab tiuxetan: CT, clinical trial
ibritumomab tiuxetan: CM, drug comparison
ibritumomab tiuxetan: PD, pharmacology
imatinib: AE, adverse drug reaction
imatinib: CT, clinical trial
imatinib: PD, pharmacology
irinotecan: CB, drug combination
l 778123
lapatinib: CT, clinical trial
lapatinib: PD, pharmacology
lonafarnib
mitoxantrone: CB, drug combination
mitoxantrone: CM, drug comparison
monoclonal antibody: AE, adverse drug reaction

monoclonal antibody: CT, clinical trial
monoclonal antibody: CB, drug combination
monoclonal antibody: CM, drug comparison
monoclonal antibody: PD, pharmacology
paclitaxel: CB, drug combination
phosphotransferase
prednisone: CB, drug combination
protein tyrosine kinase
protein tyrosine kinase inhibitor: AE, adverse drug reaction
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: CB, drug combination
protein tyrosine kinase inhibitor: PD, pharmacology
rituximab: AE, adverse drug reaction
rituximab: CT, clinical trial
rituximab: CB, drug combination
rituximab: CM, drug comparison
rituximab: PD, pharmacology
semaxanib
tipifarnib
tositumomab: PD, pharmacology
trastuzumab: AE, adverse drug reaction
trastuzumab: CB, drug combination
trastuzumab: PD, pharmacology
unindexed drug
vatalanib
vincristine: CB, drug combination

RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (alemtuzumab) 216503-57-0; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (cyclophosphamide) 50-18-0; (cytarabine) 147-94-4, 69-74-9; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (ibritumomab tiuxetan) 206181-63-7; (imatinib) 152459-95-5, 220127-57-1; (irinotecan) 100286-90-6; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lonafarnib) 193275-84-2; (mitoxantrone) 65271-80-9, 70476-82-3; (paclitaxel) 33069-62-4; (phosphotransferase) 9031-09-8, 9031-44-1; (prednisone) 53-03-2; (protein tyrosine kinase) 80449-02-1; (rituximab) 174722-31-7; (semaxanib) 186610-95-7; (tipifarnib) 192185-72-1; (tositumomab) 208921-02-2; (trastuzumab) 180288-69-1; (vatalanib) 212141-54-3, 212142-18-2; (vincristine) 57-22-7

CN ci 1033; gw 2016; imc c225; l 778123; osi 774; pki 166; ptk 787; r115777; sch 66336; sti 571; su 5416; su 6668; zd 1839

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ACCESSION NUMBER: 2003387676 EMBASE Full-text
TITLE: Lapatinib ditosylate GlaxoSmithKline.
AUTHOR: Kim T.E.; Murren J.R.
CORPORATE SOURCE: T.E. Kim, 449 S Doheny Drive, Beverley Hills, CA 90211, United States. Tracy.kim@snet.net
SOURCE: Idrugs, (1 Sep 2003) Vol. 6, No. 9, pp. 886-893.
Refs: 73
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2003
Last Updated on STN: 9 Oct 2003

AB Lapatinib ditosylate, an ErbB-2 and EGFR dual tyrosine kinase inhibitor, is being developed by GlaxoSmithKline plc for the potential treatment of solid tumors. .COPYRGT. Current Drugs.

CT Medical Descriptors:
antineoplastic activity
cancer inhibition
clinical trial
diarrhea: SI, side effect
dose response
drug bioavailability
drug blood level
drug contraindication
drug eruption: SI, side effect
drug half life
drug metabolism
drug potency
drug potentiation
drug synthesis
drug tolerability
drug toxicity
flatulence: SI, side effect
gastrointestinal symptom: SI, side effect
headache: SI, side effect
human
IC 50
liver dysfunction: SI, side effect
mucosa inflammation: SI, side effect
nonhuman
review
solid tumor: DT, drug therapy
steady state
structure activity relation

CT Drug Descriptors:
canertinib: CM, drug comparison
canertinib: PD, pharmacology
capecitabine: AE, adverse drug reaction
capecitabine: CT, clinical trial
capecitabine: CB, drug combination
capecitabine: DT, drug therapy
capecitabine: PO, oral drug administration
carboplatin: CB, drug combination
carboplatin: IT, drug interaction
carboplatin: PD, pharmacology
cetuximab: CB, drug combination
cetuximab: IT, drug interaction
cetuximab: PD, pharmacology
docetaxel: CB, drug combination
docetaxel: IT, drug interaction
docetaxel: PD, pharmacology
doxorubicin: CB, drug combination
doxorubicin: IT, drug interaction
doxorubicin: PD, pharmacology
epidermal growth factor receptor: EC, endogenous compound
erlotinib: CT, clinical trial
erlotinib: CM, drug comparison
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology

fluorouracil: DT, drug therapy
gefitinib: CB, drug combination
gefitinib: CM, drug comparison
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
growth factor receptor: EC, endogenous compound
gw 20168
irinotecan: CB, drug combination
irinotecan: DT, drug therapy
*lapatinib: CT, clinical trial
*lapatinib: CB, drug combination
*lapatinib: CM, drug comparison
*lapatinib: CR, drug concentration
*lapatinib: DO, drug dose
*lapatinib: IT, drug interaction
*lapatinib: DT, drug therapy
*lapatinib: PO, oral drug administration
*lapatinib: PK, pharmacokinetics
*lapatinib: PD, pharmacology
oxaliplatin: CB, drug combination
oxaliplatin: DT, drug therapy
*protein tyrosine kinase inhibitor: CT, clinical trial
*protein tyrosine kinase inhibitor: CB, drug combination
*protein tyrosine kinase inhibitor: CM, drug comparison
*protein tyrosine kinase inhibitor: CR, drug concentration
*protein tyrosine kinase inhibitor: DO, drug dose
*protein tyrosine kinase inhibitor: IT, drug interaction
*protein tyrosine kinase inhibitor: DT, drug therapy
*protein tyrosine kinase inhibitor: PO, oral drug administration
*protein tyrosine kinase inhibitor: PK, pharmacokinetics
*protein tyrosine kinase inhibitor: PD, pharmacology
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: CM, drug comparison
trastuzumab: IT, drug interaction
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
unclassified drug
RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (capecitabine) 154361-50-9; (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (docetaxel) 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (fluorouracil) 51-21-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (irinotecan) 100286-90-6; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (oxaliplatin) 61825-94-3; (trastuzumab) 180288-69-1
CN (1) ci 1033; (2) gw 20168; (3) gw 572016
CO (1) Pfizer; (2) Glaxo SmithKline (United Kingdom); (3) Glaxo SmithKline (United Kingdom); Bristol Myers Squibb; Imclone; Merck

L57 ANSWER 30 OF 51 EMBASE COPYRIGHT © 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003455330 EMBASE Full-text
TITLE: Therapeutic Potential of Tyrosine Kinase Inhibitors in Breast Cancer.
AUTHOR: Averbuch S.; Kcenler M.; Morris C.; Wakeling A.
CORPORATE SOURCE: Dr. S. Averbuch, AstraZeneca Pharmaceuticals, 1800 Concord Pike, Wilmington, DE 19850-5437, United States. Steven.averbuch@astrazeneca.com
SOURCE: Cancer Investigation, (2003) Vol. 21, No. 5, pp. 782-791. Refs: 75

ISSN: 0735-7907 CODEN: CINVD7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Dec 2003
Last Updated on STN: 11 Dec 2003

AB Despite recent advances in the treatment of breast cancer, survival rates for patients with metastatic breast cancer remain poor, and new treatments are still required for both hormone-dependent and hormone-independent disease. The epidermal growth factor receptor (EGFR) is a promising new target for anticancer therapy because it is commonly highly expressed in breast cancer and is implicated in the control of many aspects of tumor biology. Because expression of EGFR is inversely related to expression of the estrogen receptor (ER) and is associated with resistance to currently available breast cancer therapies, EGFR-targeted therapies may be valuable in the treatment of ER-negative tumors and endocrine-resistant, ER-positive tumors. Furthermore, the novel mechanism of action of EGFR-targeted therapies may complement the antitumor activity of existing treatment with cytotoxic agents, radiotherapy, or hormones. In this article, the small-molecule inhibitors of the tyrosine kinase activity of EGFR are discussed, with particular emphasis on the potential use of such agents at each stage of breast cancer, including a potential role in chemoprevention.

CT Medical Descriptors:
antineoplastic activity
*breast cancer: DT, drug therapy
cancer hormone therapy
cancer radiotherapy
cancer survival
clinical trial
colorectal cancer: DT, drug therapy
diarrhea: SI, side effect
head and neck cancer: DT, drug therapy
human
lung non small cell cancer: DT, drug therapy
meta analysis
metastasis: CO, complication
ovary cancer: DT, drug therapy
pancreas cancer: DT, drug therapy
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
priority journal
protein expression
rash: SI, side effect
review
CT Drug Descriptors:
4 (3 chloroanilino) 6,7 dimethoxyquinazoline
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PD, pharmacology

carboplatin: CT, clinical trial
  carboplatin: CB, drug combination
  carboplatin: DT, drug therapy
cetuximab: CT, clinical trial
  cetuximab: DT, drug therapy
  cetuximab: PD, pharmacology
cisplatin: CT, clinical trial
  cisplatin: CB, drug combination
  cisplatin: DT, drug therapy
  doxorubicin: CB, drug combination
*epidermal growth factor receptor
epidermal growth factor receptor antibody: CT, clinical trial
  epidermal growth factor receptor antibody: DT, drug therapy
  epidermal growth factor receptor antibody: PD, pharmacology
  erlotinib: AE, adverse drug reaction
erlotinib: CT, clinical trial
  erlotinib: DT, drug therapy
  erlotinib: PD, pharmacology
*estrogen receptor
fulvestrant: CT, clinical trial
  fulvestrant: CB, drug combination
  fulvestrant: DT, drug therapy
gefitinib: CT, clinical trial
  gefitinib: CB, drug combination
  gefitinib: DT, drug therapy
  gefitinib: PD, pharmacology
gemcitabine: CT, clinical trial
  gemcitabine: CB, drug combination
  gemcitabine: DT, drug therapy
icr 162: CT, clinical trial
  icr 162: DT, drug therapy
icr 62
lapatinib: CT, clinical trial
  lapatinib: DT, drug therapy
  lapatinib: PD, pharmacology
matuzumab: CT, clinical trial
  matuzumab: DT, drug therapy
  matuzumab: PD, pharmacology
mdx 210: CT, clinical trial
  mdx 210: DT, drug therapy
  mdx 210: PD, pharmacology
mdx 447: CT, clinical trial
  mdx 447: DT, drug therapy
  mdx 447: PD, pharmacology
  oxaliplatin: CB, drug combination
paclitaxel: CT, clinical trial
  paclitaxel: CB, drug combination
  paclitaxel: DT, drug therapy
panitumumab: CT, clinical trial
  panitumumab: DT, drug therapy
  panitumumab: PD, pharmacology
pelitinib: CT, clinical trial
  pelitinib: DT, drug therapy
  pelitinib: PD, pharmacology
  *protein tyrosine kinase inhibitor: DT, drug therapy
  *protein tyrosine kinase inhibitor: PD, pharmacology
  raltitrexed: CB, drug combination
tamoxifen
theraCIM h R3: CT, clinical trial
  theraCIM h R3: DT, drug therapy

theraCIM h R3: PD, pharmacology
topotecan: CB, drug combination
trastuzumab: PD, pharmacology
unclassified drug
unindexed drug

RN (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) 153436-53-4; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (fulvestrant) 129453-61-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (matuzumab) 339186-68-4; (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (panitumumab) 339177-26-3; (pelitinib) 257933-82-7; (raltitrexed) 112887-68-0; (tamoxifen) 10540-29-1; (topotecan) 119413-54-6, 123948-87-8; (trastuzumab) 180288-69-1

CN (1) ag 1478; (2) ci 1033; (3) ekb 569; (4) gw 2016; (5) icr 62; (6) imc c225; (7) iressa; (8) mdx 210; (9) mdx 447; (10) osi 774; (11) pki 166; (12) tarceva; (13) zd 1839; herceptin

CO (1) Calbiochem; (2) Pfizer; (3) Wyeth Ayerst; (4) Glaxo SmithKline; (5) Institute of Cancer Research; (6) Imclone; (7) Astra Zeneca; (8) Medarex; (9) Medarex; (10) Osi; (11) Novartis; (12) Osi; (13) Astra Zeneca; Bristol Myers Squibb; Genentech; Hoffmann La Roche; Merck

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ACCESSION NUMBER: 2003107827 EMBASE Full-text

TITLE: Discovery and biological evaluation of potent dual ErbB-2/EGFR tyrosine kinase inhibitors: 6-Thiazolylquinazolines.

AUTHOR: Gaul M.D.; Guo Y.; Affleck K.; Cockerill G.S.; Gilmer T.M.; Griffin R.J.; Guntrip S.; Keith B.R.; Knight W.B.; Mullin R.J.; Murray D.M.; Rusnak D.W.; Smith K.; Tadepalli S.; Wood E.R.; Lackey K.

CORPORATE SOURCE: K. Lackey, GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, NC 27709, United States. _acgu.e.lackey@gsk.com

SOURCE: Bioorganic and Medicinal Chemistry Letters, (Feb 2003) Vol. 13, No. 4, pp. 637-640.
Refs: 13
ISSN: 0960-894X CODEN: BMCLE8

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 27 Mar 2003
Last Updated on STN: 27 Mar 2003

AB We have identified a novel class of 6-thiazolylquinazolines as potent and selective inhibitors of both ErbB-2 and EGFR tyrosine kinase activity, with IC(50) values in the nanomolar range. These compounds inhibited the growth of both EGFR (HN5) and ErbB-2 (BT474) over-expressing human tumor cell lines in vitro. Using xenograft models of the same cell lines, we found that the compounds given orally inhibited in vivo tumor growth significantly compared with control animals. .COPYRGT. 2003 Elsevier Science Ltd. All rights reserved.

CT Medical Descriptors:
animal experiment

animal model
antineoplastic activity
article
cancer cell culture
controlled study
drug bioavailability
drug potency
drug selectivity
enzyme activity
enzyme inhibition
female
human
human cell
IC 50
mouse
nonhuman
oncogene neu
structure activity relation
CT Drug Descriptors:
antineoplastic agent: AN, drug analysis
antineoplastic agent: DV, drug development
antineoplastic agent: IV, intravenous drug administration
antineoplastic agent: PO, oral drug administration
antineoplastic agent: PK, pharmacokinetics
antineoplastic agent: PD, pharmacology
*epidermal growth factor receptor kinase
lapatinib
*protein tyrosine kinase inhibitor: AN, drug analysis
*protein tyrosine kinase inhibitor: DV, drug development
*protein tyrosine kinase inhibitor: IV, intravenous drug administration
*protein tyrosine kinase inhibitor: PO, oral drug administration
*protein tyrosine kinase inhibitor: PK, pharmacokinetics
*protein tyrosine kinase inhibitor: PD, pharmacology
*quinazoline derivative: AN, drug analysis
*quinazoline derivative: DV, drug development
*quinazoline derivative: IV, intravenous drug administration
*quinazoline derivative: PO, oral drug administration
*quinazoline derivative: PK, pharmacokinetics
*quinazoline derivative: PD, pharmacology
unclassified drug
RN (epidermal growth factor receptor kinase) 79070-06-4; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7
CN gw 572016

L57 ANSWER 32 OF 51 EMBASE COPYRIGHT © 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004005362 EMBASE Full-text
TITLE: Developmental Status of Molecular-Targeted Therapeutics against Cancers.
AUTHOR: Ejima A.; Akahane K.
CORPORATE SOURCE: Dr. A. Ejima, Med. Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd., 1-16-13 Kita-Kasai, Edogawa-ku, Tokyo 134-8630, Japan
SOURCE: Biotherapy, (Nov 2003) Vol. 17, No. 6, pp. 573-581. Refs: 23
ISSN: 0914-2223 CODEN: BITPE9
COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer

029 Clinical and Experimental Biochemistry
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
006 Internal Medicine
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
ENTRY DATE: Entered STN: 16 Jan 2004
Last Updated on STN: 16 Jan 2004

AB Along with the elucidation of the signaling events in proliferating cancer cells, pharmaceutical study on molecular-targeted therapeutics is flourishing. In particular, such molecular-targeted therapeutics as Gleevec and Iressa have proven successful in treating targeted cancers in clinics, as expected by their mechanism of action in cells. Furthermore, the recent trend is to develop many of these compounds as oral drugs for not only inpatients but also outpatients. Herein, we summarize various molecular-targeted therapeutics under clinical trials and describe the profiles and the developmental status of these compounds.

CT Medical Descriptors:
*cancer: DT, drug therapy
cancer cell
cancer patient
cell proliferation
clinical trial
drug mechanism
drug structure
*drug targeting
hospital patient
human
molecular biology
nonhuman
outpatient
outpatient department
review

CT Drug Descriptors:
2 [2 propyl 3 [3 [2 ethyl 4 (4 fluorophenyl) 5 hydroxyphenoxy]propoxy]phenoxy]benzoic acid: CT, clinical trial
2 [2 propyl 3 [3 [2 ethyl 4 (4 fluorophenyl) 5 hydroxyphenoxy]propoxy]phenoxy]benzoic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
antineoplastic agent: CT, clinical trial
antineoplastic agent: DT, drug therapy
bortezomib: CT, clinical trial
bortezomib: DT, drug therapy
canertinib: CT, clinical trial
canertinib: DT, drug therapy
cilengitide: CT, clinical trial
cilengitide: DT, drug therapy
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
flavopiridol: CT, clinical trial
flavopiridol: DT, drug therapy
fr 901228: CT, clinical trial
fr 901228: DT, drug therapy

gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
hmn 214: CT, clinical trial
hmn 214: DT, drug therapy
imatinib: CT, clinical trial
imatinib: DT, drug therapy
indisulam: CT, clinical trial
indisulam: DT, drug therapy
kw 2401: CT, clinical trial
kw 2401: DT, drug therapy
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
lonafarnib: CT, clinical trial
lonafarnib: DT, drug therapy
ly 29311
midostaurin: CT, clinical trial
midostaurin: DT, drug therapy
pelitinib: CT, clinical trial
pelitinib: DT, drug therapy
r 440: CT, clinical trial
r 440: DT, drug therapy
rpi 4610: CT, clinical trial
rpi 4610: DT, drug therapy
s 3304: CT, clinical trial
s 3304: DT, drug therapy
sorafenib: CT, clinical trial
sorafenib: DT, drug therapy
sulindac sulfone: CT, clinical trial
sulindac sulfone: DT, drug therapy
tak 165: CT, clinical trial
tak 165: DT, drug therapy
temsirolimus: CT, clinical trial
temsirolimus: DT, drug therapy
tipifarnib: CT, clinical trial
tipifarnib: DT, drug therapy
unclassified drug
unindexed drug
vandetanib: CT, clinical trial
vandetanib: DT, drug therapy
vatalinib: CT, clinical trial
vatalinib: DT, drug therapy

RN (2 [2 propyl 3 [3 [2 ethyl 4 (4 fluorophenyl) 5 hydroxyphenoxy]propoxy]phenoxy]benzoic acid) 161172-51-6; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (bortezomib) 179324-69-7, 197730-97-5; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cilengitide) 188968-51-6; (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5, 146426-40-6; (fr 901228) 128517-07-7; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (indisulam) 165668-41-7; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lonafarnib) 193275-84-2; (midostaurin) 120685-11-2; (pelitinib) 257933-82-7; (sorafenib) 284461-73-0; (sulindac sulfone) 59973-80-7; (temsirolimus) 162635-04-3, 343261-52-9; (tipifarnib) 192185-72-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3

CN (1) azd 6474; (2) bay43 9006; (3) bms 214662; (4) cci 779; (5) ekb 569; (6) gleevec; (7) iressa; (8) ly 29311; (9) r 440; (10) rpi 4610; (11) su 6668; ci 1033; fk 228; gw 572016; hmn 214; kw 2401; s 3304; tak 165; tarceva

CO (1) Astra Zeneca; (2) Bayer; (3) Bms; (4) Wyeth; (5) Wyeth; (6) Novartis; (7) Astra Zeneca; (8) Lilly; (9) Hoffmann La Roche; (10) sirna; (11) Sugen; Aton; Aventis; Cell Pathways; Glaxo SmithKline; Jansen; Merck; Millennium Pharmaceuticals; Onyx; Osi; Pfizer; Schering Plough

L57 ANSWER 33 OF 51 EMBASE COPYRIGHT © 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003488362 EMBASE Full-text
TITLE: Activation of Tyrosine Kinases in Cancer.
AUTHOR: Vlahovic G.; Crawford J.
CORPORATE SOURCE: Dr. J. Crawford, Duke University Medical Center, Box 3198, Morris Building, Durham, NC 27710, United States. Crawf006C@mc.duke.edu
SOURCE: Oncologist, (2003) Vol. 8, No. 6, pp. 531-538.
Refs: 64
ISSN: 1083-7159 CODEN: OCOLF6
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jan 2004
Last Updated on STN: 5 Jan 2004

AB Receptor and nonreceptor tyrosine kinases (TKs) have emerged as clinically useful drug target molecules for treating certain types of cancer. Epidermal growth factor receptor (EGFR)-TK is a transmembrane receptor TK that is overexpressed or aberrantly activated in the most common solid tumors, including non-small cell lung cancer and cancers of the breast, prostate, and colon. Activation of the EGFR-TK enzyme results in autophosphorylation, which drives signal transduction pathways leading to tumor growth and malignant progression. Randomized clinical trials of the EGFR-TK inhibitor gefitinib have demonstrated clinical benefits in patients with advanced non-small cell lung cancer whose disease had previously progressed on platinum-and docetaxel-based chemotherapy regimens. Bcr-Abl is a constitutively activated nonreceptor TK enzyme found in the cytoplasm of Philadelphia chromosome-positive leukemia cells. STI571 (imatinib mesylate) inhibits the Bcr-Abl TK, blocks the growth of these leukemia cells, and induces apoptosis. STI571 also inhibits other TKs, including the receptor TK c-kit, which is expressed in gastrointestinal stromal tumors. As TK inhibitors become available for clinical use, new challenges include predicting which patients are most likely to respond to these targeted TK inhibitors. Additional clinical trials are needed to develop the full potential of receptor and nonreceptor TK inhibitors for cancer treatment .

CT Medical Descriptors:
anemia: SI, side effect
bone marrow suppression: SI, side effect
*breast carcinoma: DT, drug therapy
*breast carcinoma: EP, epidemiology
*breast carcinoma: ET, etiology
clinical trial
*colon carcinoma: DT, drug therapy
*colon carcinoma: EP, epidemiology
*colon carcinoma: ET, etiology
diarrhea: SI, side effect
edema: SI, side effect
enzyme activation

gene overexpression
human
*lung non small cell cancer: DT, drug therapy
*lung non small cell cancer: EP, epidemiology
*lung non small cell cancer: ET, etiology
myalgia: SI, side effect
nausea: SI, side effect
neutropenia: SI, side effect
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
Philadelphia 1 chromosome
phosphorylation
priority journal
*prostate carcinoma: DT, drug therapy
*prostate carcinoma: EP, epidemiology
*prostate carcinoma: ET, etiology
review
side effect: SI, side effect
thrombocytopenia: SI, side effect
tumor growth
vomiting: SI, side effect
CT Drug Descriptors:
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: AE, adverse drug reaction
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
*canertinib: AE, adverse drug reaction
*canertinib: CT, clinical trial
*canertinib: DT, drug therapy
*canertinib: PD, pharmacology
*erlotinib: AE, adverse drug reaction
*erlotinib: CT, clinical trial
*erlotinib: DT, drug therapy
*erlotinib: PD, pharmacology
*gefitinib: AE, adverse drug reaction
*gefitinib: CT, clinical trial
*gefitinib: DT, drug therapy
*gefitinib: PD, pharmacology
*imatinib: AE, adverse drug reaction
*imatinib: CT, clinical trial
*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
lapatinib: AE, adverse drug reaction
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
platinum derivative: AE, adverse drug reaction
platinum derivative: CT, clinical trial
platinum derivative: DT, drug therapy
platinum derivative: PD, pharmacology
*protein tyrosine kinase: EC, endogenous compound

unclassified drug
RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (protein tyrosine kinase) 80449-02-1
CN ci 1033; gw 572016; osi 774; pki 166

L57 ANSWER 34 OF 51 EMBASE COPYRIGHT © 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003254719 EMBASE Full-text
TITLE: The development of the molecular target-based drug in the treatment for lung cancer and the significance of gefitinib.
AUTHOR: Horiike A.; Saijo N.
CORPORATE SOURCE: N. Saijo, Division of Internal Medicine, National Cancer Center Hospital, Tokyo, Japan
SOURCE: Japanese Journal of Chest Diseases, (2003) Vol. 62, No. 6, pp. 479-488.
Refs: 30
ISSN: 0385-3667 CODEN: NKYRAC
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 17 Jul 2003
CT Medical Descriptors:
article
cancer chemotherapy
clinical trial
drug efficacy
human
*lung cancer: DT, drug therapy
lung non small cell cancer: DT, drug therapy
CT Drug Descriptors:
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
canertinib: CT, clinical trial
cetuximab: CT, clinical trial
epidermal growth factor receptor
erlotinib: CT, clinical trial
*gefitinib: CT, clinical trial
*gefitinib: DT, drug therapy
imatinib
lapatinib: CT, clinical trial
matrix metalloproteinase
matrix metalloproteinase inhibitor
prinomastat
tanomastat
vasculotropin
RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (prinomastat) 192329-42-3, 195008-93-6; (tanomastat) 179545-76-7, 179545-77-8; (vasculotropin) 127464-60-2
CN ci 1033; gleevec; gw 2016; imcc 225; osi 774; pki 166; sti 571; zd 1839

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ACCESSION NUMBER: 2003425260 EMBASE Full-text
TITLE: Antibody Treatment of Breast Cancer.
AUTHOR: Tajima T.; Saitoh Y.; Suzuki Y.; Tokuda Y.
CORPORATE SOURCE: Dr. T. Tajima, Department of Surgery, Tokai University School of Medicine, Isehara, Kanagawa 259-1193, Japan
SOURCE: Biotherapy, (Sep 2003) Vol. 17, No. 5, pp. 437-446. Refs: 75
ISSN: 0914-2223 CODEN: BITPE9
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
ENTRY DATE: Entered STN: 6 Nov 2003
Last Updated on STN: 6 Nov 2003

AB Trastuzumab was introduced into clinical use in Japan in June 2001, and has been quite instrumental in improving the therapeutic results of HER2-overexpressing metastatic breast cancer. According to reports from around the world, response rates have been as high as 100% in the neoadjuvant setting and QOL for patients with metastatic disease has improved with trastuzumab-based chemotherapy. With these remarkable antitumor effects, early testing of the HER2 status of the tumor is warranted for determining the course of treatment with the highest possible potential for realizing the advantages of the application of this agent in adjuvant and/or neoadjuvant settings. With its synergistic interaction with many chemotherapeutic agents, further research is necessary to additionally explore schedules and combinations that optimize therapeutic results. Since HER2-overexpression is seen only in 20-25% of women with breast cancer, there is a need to explore other areas of targeting therapy with novel antibodies, small molecules and their combinations. Dual tyrosine kinase inhibitors and bevacizumab are among those agents that have been shown to be quite promising.

CT Medical Descriptors:
antineoplastic activity
article
*breast cancer: DT, drug therapy
cancer adjuvant therapy
*cancer therapy
drug targeting
female
gene overexpression
human
Japan
metastasis: DT, drug therapy
oncogene neu
quality of life

CT Drug Descriptors:
2 (8 hydroxy 6 methoxy 1 oxo 1h 2 benzopyran 3 yl)propionic acid
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester
ae 941
anthracycline: DT, drug therapy
*antibody: CB, drug combination

*antibody: DT, drug therapy
bevacizumab: DT, drug therapy
canertinib
capecitabine
carboplatin: CB, drug combination
carboplatin: DT, drug therapy
cetuximab
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
docetaxel: DT, drug therapy
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
epirubicin: CB, drug combination
epirubicin: DT, drug therapy
erlotinib
gefitinib
gemcitabine
imatinib
interleukin 12
lapatinib
matuzumab
n [5 (5 tert butyl 2 oxazolylmethylthio) 2 thiazolyl]isonipecotamide
n acetylsarcosylglycylvalyl dextro alloisoleucylthreonylnorvalylisoleucyla
rginylproline ethylamide
navelbine: DT, drug therapy
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
pertuzumab
protein tyrosine kinase inhibitor: DT, drug therapy
rhendostatin
sunitinib
taxane derivative: CB, drug combination
taxane derivative: DT, drug therapy
temsirolimus
*trastuzumab: CB, drug combination
*trastuzumab: DT, drug therapy
unclassified drug
unindexed drug
vandetanib

RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (bevacizumab) 216974-75-3; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (capecitabine) 154361-50-9; (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (cyclophosphamide) 50-18-0; (docetaxel) 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (epirubicin) 56390-09-1, 56420-45-2; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (imatinib) 152459-95-5, 220127-57-1; (interleukin 12) 138415-13-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (matuzumab) 339186-68-4; (n acetylsarcosylglycylvalyl dextro alloisoleucylthreonylnorvalylisoleucylarginylproline ethylamide) 251579-55-2, 251579-56-3; (navelbine) 71486-22-1; (paclitaxel) 33069-62-4; (sunitinib) 341031-54-7, 557795-19-4; (temsirolimus) 162635-04-3, 343261-52-9; (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3

CN abt 510; avastin; bms 387032; cci 779; cep 5214; cep 7055; ci 1033; emd 72000; gemzar; glivec; gw 572016; herceptin; imc c225; iressa; neovastat; nm 3; osi 774; pertuzumab; rhendostatin; sti 571; su 11248; tarceva; taxol; taxotere; tsu 68; zd 1839; zd 6474

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ACCESSION NUMBER: 2003448048 EMBASE Full-text
TITLE: Issues and progress with protein kinase inhibitors for cancer treatment.
AUTHOR: Dancey J.; Sausville E.A.
CORPORATE SOURCE: J. Dancey, Div. Of Cancer Treatment/Diagnosis, Cancer Therapy Evaluation Program, Investigational Drug Branch, 6130 Executive Blvd., Rockville, MD 20852, United States. danceyj@ctep.nci.nih.gov
SOURCE: Nature Reviews Drug Discovery, (Apr 2003) Vol. 2, No. 4, pp. 296-313.
Refs: 150
ISSN: 1474-1776 CODEN: NRDDAG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Nov 2003
Last Updated on STN: 20 Nov 2003

AB Identification of the key roles of protein kinases in cancer has led to extensive efforts to develop kinase inhibitors for the treatment of a wide range of cancers, and more than 30 such agents are now in clinical trials. Here, we consider the crucial issues in the development of kinase inhibitors for cancer, and discuss strategies to address the challenges raised by these issues in the light of preclinical and clinical experiences so far.

CT Medical Descriptors:
antineoplastic activity
breast cancer: DT, drug therapy
cancer survival
chronic myeloid leukemia: DI, diagnosis
chronic myeloid leukemia: DT, drug therapy
chronic myeloid leukemia: ET, etiology
clinical trial
drug mechanism
drug response
drug targeting
enzyme inhibition
fibrosarcoma: DT, drug therapy
gastrointestinal stromal tumor: DT, drug therapy
gene expression
human
molecular mechanics
oncogene neu
priority journal
protein targeting
review
signal transduction
CT Drug Descriptors:
1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene: CT, clinical trial
1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene: PD, pharmacology
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: CT, clinical trial
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4

difluorobenzamide: PD, pharmacology
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: PD, pharmacology
7 hydroxystaurosporine: CT, clinical trial
7 hydroxystaurosporine: PD, pharmacology
bryostatin 1: CT, clinical trial
bryostatin 1: PD, pharmacology
canertinib: CT, clinical trial
canertinib: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: PD, pharmacology
cgp 69846a: CT, clinical trial
cgp 69846a: PD, pharmacology
cgp4125
epidermal growth factor receptor: EC, endogenous compound
epidermal growth factor receptor antibody: CT, clinical trial
epidermal growth factor receptor antibody: PD, pharmacology
erlotinib: CT, clinical trial
erlotinib: PD, pharmacology
everolimus: CT, clinical trial
everolimus: PD, pharmacology
flavopiridol: CT, clinical trial
flavopiridol: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: PD, pharmacology
imatinib: DT, drug therapy
imatinib: PD, pharmacology
isis 2503: CT, clinical trial
isis 2503: PD, pharmacology
lapatinib: CT, clinical trial
lapatinib: PD, pharmacology
lonafarnib: CT, clinical trial
lonafarnib: PD, pharmacology
matuzumab
mdx 447
midostaurin: CT, clinical trial
midostaurin: PD, pharmacology
mitogen activated protein kinase kinase: EC, endogenous compound
panitumumab
pelitinib: CT, clinical trial
pelitinib: PD, pharmacology
protein kinase: EC, endogenous compound
*protein kinase inhibitor: CT, clinical trial
*protein kinase inhibitor: DT, drug therapy
*protein kinase inhibitor: PD, pharmacology
Raf protein: EC, endogenous compound
rapamycin: CT, clinical trial
rapamycin: PD, pharmacology
Ras protein: EC, endogenous compound
rh3
temsirolimus: CT, clinical trial
temsirolimus: PD, pharmacology
tipifarnib: CT, clinical trial
tipifarnib: PD, pharmacology
trastuzumab: DT, drug therapy
unclassified drug
unindexed drug
RN (1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene) 109511-58-2;

(2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide) 212631-79-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (7 hydroxystaurosporine) 112953-11-4; (bryostatin 1) 83314-01-6; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (cgp 69846a) 177075-18-2; (erlotinib) 183319-69-9, 183321-74-6; (everolimus) 159351-69-6; (flavopiridol) 131740-09-5, 146426-40-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (isis 2503) 149957-14-2; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lonafarnib) 193275-84-2; (matuzumab) 339186-68-4; (midostaurin) 120685-11-2; (mitogen activated protein kinase kinase) 142805-58-1; (panitumumab) 339177-26-3; (pelitinib) 257933-82-7; (protein kinase) 9026-43-1; (rapamycin) 53123-88-9; (temsirolimus) 162635-04-3, 343261-52-9; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1

CN (1) abx egf; (2) bms 214662; (3) cci 779; (4) cgp4125; (5) ekb 569; (6) emd 72000; (7) erbitux; (8) gleevec; (9) glivec; (10) gw2016; (11) herceptin; (12) hmr 1275; (13) iressa; (14) isis 5132; (15) mdx 447; (16) mdx 447; (17) pd 183805; (18) pd 184352; (19) rad001; (20) rh3; (21) sch 66336; (22) tarceva; (23) u 0126; (24) ucn 01; (25) zd 1839; sti 571

CO (1) Abgenix; (2) Bristol Myers Squibb; (3) Wyeth; (4) Novartis; (5) Wyeth; (6) Merck; (7) Imclone; (8) Novartis; (9) Novartis; (10) Glaxo SmithKline; (11) Genentech; (12) Aventis; (13) Astra Zeneca; (14) Isis; (15) Medarex; (16) Merck; (17) Pfizer; (18) Pfizer; (19) Novartis; (20) York Medical Bioscience; (21) Schering Plough; (22) Osi; (23) Promega; (24) Kyowa Hakko Kogyo; (25) Astra Zeneca; GPC Biotek; Johnson and Johnson

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ACCESSION NUMBER: 2003375105 EMBASE Full-text
TITLE: Molecular target-based cancer therapy: Tyrosine kinase inhibitors.
AUTHOR: Tamura K.; Fukuoka M.
CORPORATE SOURCE: K. Tamura, Department of Medical Oncology, Kinki University School of Medicine, 377-2 Ohno-higashi, Osaka-Sayama, Osaka 589-8511, Japan. tamura@med.kindai.ac.jp
SOURCE: International Journal of Clinical Oncology, (Aug 2003) Vol. 8, No. 4, pp. 207-211.
Refs: 19
ISSN: 1341-9625 CODEN: IJCOF6
COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 2 Oct 2003

AB Improved understanding of tumor biology has led to the identification of numerous growth factors that are involved in malignant transformation and tumor progression. Many of these factors induce cellular responses through receptors with intrinsic tyrosine kinase (TK) activity. Therefore, inhibiting the activity of TK receptors is one of the ways to effectively block the disordered proliferation of cancer that arises from these pathways. The human epidermal growth factor receptor (HER) family is overexpressed or dysfunctional in many human malignancies. Therefore, these receptors have been identified as targets for cancer therapy . Several agents have been

developed that reversibly or irreversibly inhibit one, two, or all of the HER receptors. Iressa and Tarceva are HER1-specific TK inhibitors that are in advanced development. The large phase II study of Iressa (IDEAL1) in patients with non-small-cell lung cancer (NSCLC) in whom previous platinum-based therapy has failed, found that the median survival time (MST) was 7.6 months, which was no less than that with Docetaxel treatment. Other dual or pan-HER, reversible or irreversible, TK inhibitors are being investigated in phase I trials. Early data show that they are generally well tolerated and have provided evidence of against activity tumors. HER-TK inhibitors are likely to have a substantial impact on the treatment of cancer patients.

CT Medical Descriptors:
acne: SI, side effect
*cancer chemotherapy
cancer combination chemotherapy
cancer growth
cancer survival
chemotherapy induced emesis: SI, side effect
clinical trial
diarrhea: SI, side effect
dose response
drug eruption: SI, side effect
drug hypersensitivity: SI, side effect
drug mechanism
drug targeting
drug tolerability
enzyme activity
fatigue: SI, side effect
human
liver toxicity: SI, side effect
lung non small cell cancer: DT, drug therapy
lung non small cell cancer: RT, radiotherapy
malignant transformation
nausea: SI, side effect
priority journal
protein expression
protein family
review
survival time
thrombocytopenia: SI, side effect
treatment outcome

CT Drug Descriptors:
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: AE, adverse drug reaction
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DO, drug dose
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PO, oral drug administration
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PK, pharmacokinetics
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
canertinib: AE, adverse drug reaction
canertinib: CT, clinical trial
canertinib: DO, drug dose
canertinib: DT, drug therapy
canertinib: PD, pharmacology

carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: DT, drug therapy
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: DT, drug therapy
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
epidermal growth factor receptor: EC, endogenous compound
erlotinib: AE, adverse drug reaction
erlotinib: CT, clinical trial
erlotinib: CB, drug combination
erlotinib: DO, drug dose
erlotinib: DT, drug therapy
erlotinib: PO, oral drug administration
erlotinib: PK, pharmacokinetics
erlotinib: PD, pharmacology
gefitinib: AE, adverse drug reaction
gefitinib: CT, clinical trial
gefitinib: CB, drug combination
gefitinib: DO, drug dose
gefitinib: DT, drug therapy
gefitinib: PO, oral drug administration
gefitinib: PD, pharmacology
gemcitabine: CT, clinical trial
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
lapatinib: CT, clinical trial
lapatinib: DO, drug dose
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
pelitinib: CT, clinical trial
pelitinib: DO, drug dose
pelitinib: DT, drug therapy
pelitinib: PD, pharmacology
platinum derivative: CT, clinical trial
platinum derivative: CB, drug combination
platinum derivative: DT, drug therapy
protein tyrosine kinase: EC, endogenous compound
*protein tyrosine kinase inhibitor: AE, adverse drug reaction
*protein tyrosine kinase inhibitor: CT, clinical trial
*protein tyrosine kinase inhibitor: CB, drug combination
*protein tyrosine kinase inhibitor: DO, drug dose
*protein tyrosine kinase inhibitor: DT, drug therapy
*protein tyrosine kinase inhibitor: PO, oral drug administration
*protein tyrosine kinase inhibitor: PK, pharmacokinetics
*protein tyrosine kinase inhibitor: PD, pharmacology
taxane derivative: CT, clinical trial
taxane derivative: CB, drug combination
taxane derivative: DT, drug therapy
unclassified drug

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carboplatin) 41575-94-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (paclitaxel)

33069-62-4; (pelitinib) 257933-82-7; (protein tyrosine kinase) 80449-02-1
CN (1) ci 1033; (2) ekb 569; (3) gw 572016; (4) iressa; (5) osi 774; (6) osi 774; (7) pki 166; (8) tarceva; (9) tarceva; (10) zd 1839
CO (1) Pfizer; (2) Wyeth Ayerst; (3) Glaxo SmithKline; (4) Astra Zeneca; (5) Genentech; (6) Osi; (7) Novartis; (8) Genentech; (9) Osi; (10) Astra Zeneca

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ACCESSION NUMBER: 2004009374 EMBASE Full-text
TITLE: Development of new agents for the treatment of advanced colorectal cancer.
AUTHOR: Lewis N.L.; Meropol N.J.
CORPORATE SOURCE: Dr. N.L. Lewis, Division of Medical Science, Fox Chase Cancer Center, 7701 Burholme Ave., Philadelphia, PA 19111, United States. N_lewis@fccc.de
SOURCE: Clinical Colorectal Cancer, (Nov 2003) Vol. 3, No. 3, pp. 154-164.
Refs: 106
ISSN: 1533-0028 CODEN: CCCLCF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2004
Last Updated on STN: 16 Jan 2004

AB During the past decade, there have been several significant advances in the treatment of metastatic colorectal cancer. These include the introduction of the cytotoxic agents capecitabine, irinotecan, and oxaliplatin. Given their diverse mechanisms of action and toxicity profiles, combinations of fluoropyrimidines, irinotecan, and oxaliplatin have proven feasible and have improved patient outcomes compared with 5-fluorouracil alone. Recently, improved understanding of the biology of colorectal cancer has led to the identification of new molecular targets and the development of pharmacologic agents that hold promise for greater tumor selectivity than traditional cytotoxic agents. Two approaches with early indications of clinical activity against colorectal cancer are inhibition of epidermal growth factor receptor signaling and inhibition of the vascular endothelial growth factor pathway. Furthermore, biochemical and genetic profiling of individual tumors, as well as patient genotyping, may ultimately guide clinicians in making rational treatment decisions based on predicted antitumor efficacy or toxicity of selected agents. This article reviews these recent advances in the systemic treatment of colorectal cancer, including discussion of promising agents in clinical development.

CT Medical Descriptors:
advanced cancer: DT, drug therapy
artery thrombosis: SI, side effect
bone marrow toxicity: SI, side effect
clinical trial
*colorectal cancer: DT, drug therapy
drug bioavailability
drug efficacy
drug indication
drug mechanism
drug metabolism

drug potentiation
drug selectivity
drug targeting
dysesthesia: SI, side effect
feasibility study
febrile neutropenia: SI, side effect
folliculitis: SI, side effect
gene expression profiling
genotype
human
larynx spasm: SI, side effect
medical decision making
metastasis: DT, drug therapy
monotherapy
nausea: SI, side effect
nephrotoxicity: SI, side effect
paresthesia: SI, side effect
peripheral neuropathy: SI, side effect
practice guideline
rash: SI, side effect
receptor blocking
review
signal transduction
treatment outcome
vein thrombosis: SI, side effect
vomiting: SI, side effect

CT Drug Descriptors:
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: AE, adverse drug reaction
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: DV, drug development
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: PD, pharmacology
7 ethyl 10 hydroxycamptothecin: PK, pharmacokinetics
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: CM, drug comparison
bevacizumab: DV, drug development
bevacizumab: DO, drug dose
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
canertinib: AE, adverse drug reaction
canertinib: DV, drug development
canertinib: DT, drug therapy
canertinib: PD, pharmacology
capecitabine: CT, clinical trial
capecitabine: CB, drug combination
capecitabine: CM, drug comparison
capecitabine: DO, drug dose
capecitabine: DT, drug therapy
capecitabine: PO, oral drug administration
capecitabine: PK, pharmacokinetics
capecitabine: PD, pharmacology
carboplatin: AE, adverse drug reaction
carboplatin: DT, drug therapy

celecoxib: CT, clinical trial
  celecoxib: DT, drug therapy
  celecoxib: PD, pharmacology
  cetuximab: AE, adverse drug reaction
cetuximab: CT, clinical trial
  cetuximab: DO, drug dose
  cetuximab: DT, drug therapy
  cetuximab: IV, intravenous drug administration
  cetuximab: PD, pharmacology
  cisplatin: AE, adverse drug reaction
  cisplatin: DT, drug therapy
  cytotoxic agent: AE, adverse drug reaction
cytotoxic agent: CT, clinical trial
  cytotoxic agent: CB, drug combination
  cytotoxic agent: CM, drug comparison
  cytotoxic agent: DO, drug dose
  cytotoxic agent: IT, drug interaction
  cytotoxic agent: DT, drug therapy
  cytotoxic agent: IV, intravenous drug administration
  cytotoxic agent: PO, oral drug administration
  cytotoxic agent: PK, pharmacokinetics
  cytotoxic agent: PD, pharmacology
epidermal growth factor receptor: EC, endogenous compound
  epidermal growth factor receptor antibody: AE, adverse drug reaction
epidermal growth factor receptor antibody: CT, clinical trial
  epidermal growth factor receptor antibody: DO, drug dose
  epidermal growth factor receptor antibody: DT, drug therapy
  epidermal growth factor receptor antibody: PK, pharmacokinetics
  epidermal growth factor receptor antibody: PD, pharmacology
  erlotinib: AE, adverse drug reaction
erlotinib: CT, clinical trial
  erlotinib: CB, drug combination
  erlotinib: DV, drug development
  erlotinib: DT, drug therapy
  erlotinib: PO, oral drug administration
  erlotinib: PK, pharmacokinetics
  erlotinib: PD, pharmacology
  fluoropyrimidine derivative: CB, drug combination
  fluoropyrimidine derivative: CM, drug comparison
  fluoropyrimidine derivative: DT, drug therapy
  fluorouracil: AE, adverse drug reaction
fluorouracil: CT, clinical trial
  fluorouracil: CB, drug combination
  fluorouracil: CM, drug comparison
  fluorouracil: DO, drug dose
  fluorouracil: IT, drug interaction
  fluorouracil: DT, drug therapy
  fluorouracil: IV, intravenous drug administration
  fluorouracil: PD, pharmacology
  folinic acid: AE, adverse drug reaction
folinic acid: CT, clinical trial
  folinic acid: CB, drug combination
  folinic acid: CM, drug comparison
  folinic acid: DO, drug dose
  folinic acid: DT, drug therapy
  gefitinib: AE, adverse drug reaction
gefitinib: CT, clinical trial
  gefitinib: CB, drug combination
  gefitinib: DT, drug therapy

gefitinib: PO, oral drug administration
gefitinib: PK, pharmacokinetics
gefitinib: PD, pharmacology
irinotecan: AE, adverse drug reaction
irinotecan: CT, clinical trial
irinotecan: CB, drug combination
irinotecan: CM, drug comparison
irinotecan: DO, drug dose
irinotecan: DT, drug therapy
irinotecan: IV, intravenous drug administration
lapatinib: AE, adverse drug reaction
lapatinib: DV, drug development
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
matuzumab
nonsteroid _acques_ve_matory agent: CT, clinical trial
nonsteroid _acques_ve_matory agent: DT, drug therapy
nonsteroid _acques_ve_matory agent: PD, pharmacology
oxaliplatin: AE, adverse drug reaction
oxaliplatin: CT, clinical trial
oxaliplatin: CB, drug combination
oxaliplatin: CM, drug comparison
oxaliplatin: DO, drug dose
oxaliplatin: IT, drug interaction
oxaliplatin: DT, drug therapy
pelitinib: AE, adverse drug reaction
pelitinib: DV, drug development
pelitinib: DT, drug therapy
pelitinib: PD, pharmacology
placebo
prostaglandin synthase inhibitor: PD, pharmacology
sulindac: CT, clinical trial
sulindac: DT, drug therapy
sulindac: PD, pharmacology
vasculotropin: EC, endogenous compound
vasculotropin inhibitor: DT, drug therapy
vasculotropin inhibitor: PD, pharmacology

RN (7 ethyl 10 hydroxycamptothecin) 86639-52-3; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (bevacizumab) 216974-75-3; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (capecitabine) 154361-50-9; (carboplatin) 41575-94-4; (celecoxib) 169590-42-5; (cetuximab) 205923-56-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (erlotinib) 183319-69-9, 183321-74-6; (fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (irinotecan) 100286-90-6; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (matuzumab) 339186-68-4; (oxaliplatin) 61825-94-3; (pelitinib) 257933-82-7; (sulindac) 38194-50-2; (vasculotropin) 127464-60-2

CN aspirin; ci 1033; ekb 569; emd 72000; gw 2016; osi 774; pki 166; sn 38; tarceva

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ACCESSION NUMBER: 2002442476 EMBASE Full-text
TITLE: Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs): Simple drugs with a complex mechanism of action?.
AUTHOR: Normanno N.; Maiello M.R.; De Luca A.
CORPORATE SOURCE: N. Normanno, Oncologia Sperimentale D, INT-Fondazione Pascale, Via Summola 3, 80131 Naples, Italy.

nicnorm@yahoo.com

SOURCE: Journal of Cellular Physiology, (1 Jan 2003) Vol. 194, No. 1, pp. 13-19.
Refs: 39
ISSN: 0021-9541 CODEN: JCLLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Dec 2002
Last Updated on STN: 27 Dec 2002

AB A range of target-based agents for the treatment of solid tumors are in development. The epidermal growth factor receptor (EGFR) has been identified as a relevant target as it is involved in regulating several cellular functions important in the proliferation and survival of cancer cells, is commonly expressed at high levels in a range of tumors, and high expression is often related to poor prognosis. EGFR is a member of the ErbB family of receptors which also includes ErbB-2, ErbB-3, and ErbB-4. These receptors form _acques of the same type (homodimers) or with other family members (heterodimers), each combination resulting in different downstream effects. Some of the most advanced targeted agents in development are the EGFR tyrosine kinase inhibitors (EGFR-TKIs), of which ZD1839 ('Iressa') is an example. In Phase II monotherapy trials, oral ZD1839 was well tolerated and demonstrated clinically meaningful antitumor activity and symptom relief in pretreated patients with advanced NSCLC. Preclinical studies have suggested that the antitumor activity of ZD1839 does not depend on the level of EGFR expression. Furthermore, in addition to an effect on EGFR signaling, treatment with ZD1839 as well as with other quinazoline EGFR-TKIs, may also affect signaling of other ErbB family members. EGFR-TKIs have been shown in preclinical studies to increase the efficacy of cytotoxic drugs and Phase III trials of such combinations are ongoing. On the basis that different signal transduction pathways contribute to the control of tumor growth, future therapeutic approaches are likely to involve combination of different targeted agents. .COPYRGT. 2002 Wiley-Liss, Inc.

CT Medical Descriptors:
antineoplastic activity
cancer cell
cancer inhibition
cancer survival
cell function
cell proliferation
clinical trial
drug activity
drug mechanism
drug sensitivity
drug tolerability
human
lung non small cell cancer: DT, drug therapy
monotherapy
nonhuman
priority journal
prognosis
protein expression
receptor blocking
review
signal transduction

solid tumor: DT, drug therapy
target cell
treatment outcome
CT Drug Descriptors:
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
antibody: CT, clinical trial
antibody: CB, drug combination
antibody: DT, drug therapy
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PO, oral drug administration
*antineoplastic agent: PD, pharmacology
canertinib: CT, clinical trial
_acque
*epidermal growth factor receptor: EC, endogenous compound
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
lapatinib: CT, clinical trial
pelitinib: CT, clinical trial
protein tyrosine kinase: EC, endogenous compound
*receptor blocking agent: CT, clinical trial
*receptor blocking agent: CB, drug combination
*receptor blocking agent: DT, drug therapy
*receptor blocking agent: PO, oral drug administration
*receptor blocking agent: PD, pharmacology
RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (pelitinib) 257933-82-7; (protein tyrosine kinase) 80449-02-1
CN ci 1033; ekb 569; gw 2016; pki 166; tarceva; zd 1839

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ACCESSION NUMBER:	2003437326 EMBASE Full-text
TITLE:	Targeting RAS _acques_v pathways in cancer therapy .
AUTHOR:	Downward J.
CORPORATE SOURCE:	J. Downward, Cancer Research UK, London Research Institute, 44 Lincoln's Inn Fields, London WC2A 3PX, United Kingdom. Julian.downward@cancer.org.uk
SOURCE:	Nature Reviews Cancer, (Jan 2003) Vol. 3, No. 1, pp. 11-22. Refs: 87 ISSN: 1474-175X CODEN: NRCAC4
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; General Review; (Review)
FILE SEGMENT:	016 Cancer 030 Clinical and Experimental Pharmacology 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 13 Nov 2003 Last Updated on STN: 13 Nov 2003

AB The RAS proteins control _acques_v pathways that are key regulators of several aspects of normal cell growth and malignant transformation. They are aberrant in most human tumours due to activating mutations in the RAS genes themselves

or to alterations in upstream or downstream _acques_v components. Rational therapies that target the RAS pathways might inhibit tumour growth, survival and spread. Several of these new therapeutic agents are showing promise in the clinic and many more are being developed.

CT Medical Descriptors:
cancer inhibition
*cancer therapy
drug activity
drug efficacy
enzyme inhibition
gene mutation
priority journal
protein processing
review
signal transduction

CT Drug Descriptors:
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine
antineoplastic agent
antisense oligonucleotide
canertinib
cetuximab
cgp 69846a
erlotinib
everolimus
gefitinib
growth factor receptor
imatinib
isis 2503
l 778123
lapatinib
lonafarnib
pelitinib
phosphotransferase inhibitor: PD, pharmacology
pk 1116
protein farnesyltransferase inhibitor: PD, pharmacology
protein kinase B
*Ras protein
sorafenib
temsirolimus
tipifarnib
trastuzumab
unclassified drug
zanestra

RN (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide) 212631-79-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (cgp 69846a) 177075-18-2; (erlotinib) 183319-69-9, 183321-74-6; (everolimus) 159351-69-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (isis 2503) 149957-14-2; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lonafarnib) 193275-84-2; (pelitinib) 257933-82-7; (protein kinase B) 148640-14-6; (sorafenib) 284461-73-0; (temsirolimus) 162635-04-3, 343261-52-9; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1

CN (1) ci 1033; (2) ekb 569; (3) gw 2016; (4) pk 1116; (5) tarceva; bay 43 9006; bms 214662; cci 779; erbitux; glivec; herceptin; iressa; isis 2503; isis 5132; l 778123; pd 184352; rad 001; sarasar; zanestra

CO (1) Pfizer; (2) Genetics Institute; (3) Glaxo SmithKline; (4) Novartis; (5) Osi

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ACCESSION NUMBER: 2003508973 EMBASE Full-text
TITLE: Signal Events: Cell Signal Transduction and Its Inhibition in Cancer.
AUTHOR: Rowinsky E.K.
CORPORATE SOURCE: Dr. E.K. Rowinsky, Institute for Drug Development, Cancer Therapy and Research Center, Zeller Building, 7979 Wurzbach Road, San Antonio, TX 78229, United States. erowinsk@saci.org
SOURCE: Oncologist, (2003) Vol. 8, No. SUPPL. 3, pp. 5-17. Refs: 61
ISSN: 1083-7159 CODEN: OCOLF6
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jan 2004
Last Updated on STN: 5 Jan 2004

AB Signal transduction refers to communication processes used by regulatory molecules to mediate the essential cell processes of growth, differentiation, and survival. Signal transduction elements interact through complex biochemically related networks. Aberrations in signal transduction elements can lead to increased proliferative potential, sustained angiogenesis, tissue invasion and metastasis, and apoptosis inhibition. Most human neoplasms have aberrant signal transduction elements. Several compounds that target aberrant signal transduction elements, such as those in the ErbB family of tyrosine kinase receptors and mammalian target of rapamycin, are in development. To date, commercially available signal-transduction-targeting compounds include trastuzumab, a monoclonal antibody against the ErbB-2 receptor for the treatment of metastatic breast cancer overexpressing the ErbB-2 (HER-2) receptor, and gefitinib, an inhibitor of the ErbB-1 receptor tyrosine kinase that recently received regulatory approval for the treatment of patients with non-small cell lung cancer. In contrast to traditional cytotoxic treatments, although signal transduction inhibitors are capable of inducing tumor regression, particularly in malignancies that are principally driven by specific target aberrations, preclinical and early clinical investigations suggest that their predominant beneficial effects are growth inhibitory in nature; therefore, new clinical trial designs and evaluation end points may be required to ultimately assess their value. Prospective profiling of patients and tumors to determine treatment response is also essential to the success of these clinical trials. However, responsiveness to these novel therapies is dependent on a multitude of factors that ultimately determine the robustness and quality of the downstream response.

CT Medical Descriptors:
bladder cancer: DT, drug therapy
breast cancer: DT, drug therapy
*cancer cell
cancer research
cancer therapy
cell differentiation
cell growth

cell survival
clinical trial
colorectal cancer: DT, drug therapy
conference paper
continuing education
drug targeting
head and neck cancer: DT, drug therapy
human
human cell
kidney cancer: DT, drug therapy
lung non small cell cancer: DT, drug therapy
oncogene neu
oncology
ovary cancer: DT, drug therapy
pancreas cancer: DT, drug therapy
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
priority journal
prostate cancer: DT, drug therapy
quality of life
side effect: SI, side effect
*signal transduction
treatment outcome
uterine cervix cancer: DT, drug therapy
CT Drug Descriptors:
ar 23573: DV, drug development
ar 23573: PD, pharmacology
canertinib: DV, drug development
canertinib: PD, pharmacology
*cetuximab: CT, clinical trial
*cetuximab: DT, drug therapy
*cetuximab: PD, pharmacology
chimeric antibody: CT, clinical trial
chimeric antibody: DT, drug therapy
chimeric antibody: PD, pharmacology
docetaxel: DT, drug therapy
emd 7200: CT, clinical trial
emd 7200: DT, drug therapy
emd 7200: PD, pharmacology
erlotinib: DT, drug therapy
everolimus: DV, drug development
everolimus: PD, pharmacology
*gefitinib: DT, drug therapy
*gefitinib: PD, pharmacology
h r3
human monoclonal antibody: CT, clinical trial
human monoclonal antibody: DT, drug therapy
human monoclonal antibody: PD, pharmacology
immunoglobulin G antibody: CT, clinical trial
immunoglobulin G antibody: DT, drug therapy
immunoglobulin G antibody: PD, pharmacology
lapatinib: DV, drug development
lapatinib: PD, pharmacology
mdx 447: CT, clinical trial
mdx 447: DT, drug therapy
mdx 447: PD, pharmacology
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
panitumumab

pelitinib: DV, drug development
pelitinib: PD, pharmacology
phosphatidylinositol 3,4,5 trisphosphate 3 phosphatase
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
rapamycin: DV, drug development
rapamycin: IV, intravenous drug administration
rapamycin: PD, pharmacology
temsirolimus: AE, adverse drug reaction
temsirolimus: CT, clinical trial
temsirolimus: AD, drug administration
temsirolimus: DV, drug development
temsirolimus: DO, drug dose
temsirolimus: DT, drug therapy
temsirolimus: IV, intravenous drug administration
temsirolimus: PD, pharmacology
*trastuzumab: CT, clinical trial
*trastuzumab: DT, drug therapy
*trastuzumab: PD, pharmacology
unclassified drug

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9, 183321-74-6; (everolimus) 159351-69-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (panitumumab) 339177-26-3; (pelitinib) 257933-82-7; (rapamycin) 53123-88-9; (temsirolimus) 162635-04-3, 343261-52-9; (trastuzumab) 180288-69-1

CN (1) abx egf; (2) ar 23573; (3) cci 779; (4) ekb 569; (5) emd 7200; (6) erbitux; (7) gw 572016; (8) herceptin; (9) iressa; (10) mdx 447; (11) rad 001; (12) rapamune; (13) tarceva; ci 1033; h r3

CO (1) Abgenix (United States); (2) Ariad (United States); (3) Novartis (United States); (4) Wyeth Ayerst (United States); (5) Merck (Germany); (6) Imclone (United States); (7) Glaxo SmithKline (United Kingdom); (8) Genentech (United States); (9) Astra Zeneca (United States); (10) Medarex (United States); (11) Novartis (United States); (12) Wyeth (United States); (13) Osi (United States)

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ACCESSION NUMBER:	2003111438 EMBASE Full-text
TITLE:	The epidermal growth factor receptor-tyrosine kinase: A promising therapeutic target in solid tumors.
AUTHOR:	Ritter C.A.; Arteaga C.L.
CORPORATE SOURCE:	Dr. C.L. Arteaga, Division of Hematology-Oncology, Vanderbilt Univ. School of Medicine, 777 PRB, 2220 Pierce Ave, Nashville, TN 37232-6307, United States
SOURCE:	Seminars in Oncology, (Feb 2003) Vol. 30, No. 1 SUPPL. 1, pp. 3-11. Refs: 69 ISSN: 0093-7754 CODEN: SOLGAV
COUNTRY:	United States
DOCUMENT TYPE:	Journal; General Review; (Review)
FILE SEGMENT:	016 Cancer 030 Clinical and Experimental Pharmacology 037 Drug Literature Index 038 Adverse Reactions Titles
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 27 Mar 2003

Last Updated on STN: 27 Mar 2003

AB The overexpression and aberrant function of the epidermal growth factor receptor (EGFR) and its ligands in several human carcinomas have provided a rationale for targeting this signaling network with novel treatment approaches. The epidermal growth factor receptor-tyrosine kinase (EGFR-TK) is a selective target for inhibiting cancer because it is activated in many tumor cells, yet is strictly controlled in normal cells. The EGFR-TK initiates diverse signal transduction pathways in tumor cells that have a profound effect on their biology. Activation of the EGFR-TK provides signals that drive dysregulated proliferation, invasion and metastasis, angiogenesis, and enhanced cell survival. Therefore, the EGFR-TK is a promising drug target for many types of solid tumors, and its inhibition has potential in both the treatment and prevention of these neoplasias. Based on the structure and function of the EGFR, two antireceptor therapeutic strategies have been developed. The first strategy uses humanized monoclonal antibodies generated against the receptors ligand-binding, extracellular domain. These antibodies block binding of receptor-activiting ligands and, in some cases, can induce receptor endocytosis and downregulation. The second approach uses small molecules that compete with adenosine triphosphate for binding to the receptor's kinase pocket, thus blocking receptor activation and the transduction of postreceptor signals. Early clinical studies suggest that both of these approaches, either alone or in combination with standard anticancer therapies, are well tolerated and can induce clinical responses and tumor stabilization in a variety of common carcinomas. ZD 1839 (Iressa; AstraZeneca Pharmaceuticals LP, Wilmington, DE) is the EGFR-TK inhibitor furthest along in clinical development, and it is currently being investigated in a variety of solid tumors, Including non-small-cell lung cancer.

CT Medical Descriptors:

angiogenesis
  breast cancer: DT, drug therapy
  cancer combination chemotherapy
cancer invasion
cell proliferation
cell survival
  chronic myeloid leukemia: DT, drug therapy
clinical trial
down regulation
  drug half life
  drug synthesis
  drug targeting
  drug tolerability
endocytosis
enzyme activation
gastrointestinal toxicity: SI, side effect
human
ligand binding
  lung non small cell cancer: DT, drug therapy
metastasis: CO, complication
nonhuman
oncogene neu
priority journal
protein domain
protein expression
receptor blocking
review
signal transduction
skin toxicity: SI, side effect
  *solid tumor: DT, drug therapy

CT Drug Descriptors:

canertinib: PD, pharmacology
cetuximab: PD, pharmacology
epidermal growth factor receptor antibody: PD, pharmacology
*epidermal growth factor receptor kinase: EC, endogenous compound
epidermal growth factor receptor kinase inhibitor: AE, adverse drug reaction
epidermal growth factor receptor kinase inhibitor: CT, clinical trial
epidermal growth factor receptor kinase inhibitor: DT, drug therapy
epidermal growth factor receptor kinase inhibitor: PO, oral drug administration
epidermal growth factor receptor kinase inhibitor: PK, pharmacokinetics
epidermal growth factor receptor kinase inhibitor: PD, pharmacology
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
imatinib: DT, drug therapy
imatinib: PD, pharmacology
lapatinib: PD, pharmacology
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
pelitinib: PD, pharmacology
protein tyrosine kinase inhibitor: AE, adverse drug reaction
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PO, oral drug administration
protein tyrosine kinase inhibitor: PK, pharmacokinetics
protein tyrosine kinase inhibitor: PD, pharmacology
quinazoline derivative: CT, clinical trial
quinazoline derivative: DT, drug therapy
quinazoline derivative: PD, pharmacology
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
unclassified drug

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (paclitaxel) 33069-62-4; (pelitinib) 257933-82-7; (trastuzumab) 180288-69-1

CN (1) gleevec; (2) iressa; (3) sti 571; (4) zd 1839; c 225; ci 1033; ekb 569; gw 2016; osi 774

CO (1) Novartis (United States); (2) Astra Zeneca (United States); (3) Novartis (United States); (4) Astra Zeneca (United States)

ACCESSION NUMBER: 2003274438 EMBASE Full-text

TITLE: Novel approaches with targeted therapies in bladder cancer: Therapy of bladder cancer by blockade of the epidermal growth factor receptor family.

AUTHOR: Bellmunt J.; Hussain M.; Dinney C.P.

CORPORATE SOURCE: J. Bellmunt, Medical Oncology Service, Hosp. Gen.

Universitari Vall d'H., P. Vall d'Hebron 119-129, 08035 Barcelona, Spain. bellmunt@hg.vhebron.es
SOURCE: Critical Reviews in Oncology/Hematology, (27 Jun 2003) Vol. 46, No. SUPPL., pp. S85-S104.
Refs: 207
ISSN: 1040-8428 CODEN: CCRHEC
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2003
Last Updated on STN: 24 Jul 2003

AB The improved understanding of the molecular biology of urothelial malignancies is helping to define the role of new targets and prognostic indices that can direct the most appropriate choice of treatment for advanced disease. Many human tumors express high levels of growth factors and their receptors that can be used as potential therapeutical targets. Tyrosine-kinase receptors, including many growth factor receptors such the receptors for epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and Her2/neu, have been found overexpressed in urothelial tumors. For many of these growth factor receptors, the degree of expression has been associated with the progression of cancer and a poor prognosis. Among the best studied growth factor receptors are the two members of EGF receptor familiy EGFr (ErbB-1), and Her2/neu (ErbB-2). Several preclinical studies in bladder cancer models, have confirmed that systemic administration of growth factor inhibitors inhibits the growth and metastasis of human transitional cell carcinoma established in the bladder wall of athymic nude mice. Additional studies indicate that therapy with EGFR inhibitors enhances the activity of conventional cytoreductive chemotherapeutic agents, in part by inhabiting tumor cell proliferation, angiogenesis, and inducing apoptosis. Novel targeted therapy hold promise to improve the current results of bladder cancer treatment. Based on the success seen with anti-HER2 monoclonal antibodies (Herceptin®) and the promising results with EGFR targeted agents (IMC-C225 Cetuximab®, ZD1389 Iressa®, OSI-774 Tarceva®, GW 57016) in other tumor types, and based on the results obtained in preclinical models, there is a great interest in assessing these agents in patients with bladder cancer. Several trials are now ongoing testing these new agents alone or in combination with chemotherapy in bladder cancer patients. The integration of these newer biologic agents, probably to supplement rather than to supplant chemotherapeutic drugs, should be a primary direction of research with the objective to interfere with multiple aspects of bladder cancer progression. However, the value of integration of biologically targeted agents into combined modality treatment for patients with bladder cancer has still to be proven.

CT Medical Descriptors:
angiogenesis
*bladder carcinoma: DT, drug therapy
cancer growth
cell death
cell proliferation
clinical trial
conference paper
gene targeting
human
metastasis inhibition
nonhuman

protein expression
signal transduction
CT Drug Descriptors:
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: DV, drug development
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: DT, drug therapy
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: CT, clinical trial
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3
d]pyrimidine: PD, pharmacology
bibx 1382
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PD, pharmacology
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: DT, drug therapy
carboplatin: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: DT, drug therapy
cisplatin: PD, pharmacology
ekb 56
emd 7200
*epidermal growth factor receptor: EC, endogenous compound
*epidermal growth factor receptor antibody: CT, clinical trial
*epidermal growth factor receptor antibody: DV, drug development
*epidermal growth factor receptor antibody: DT, drug therapy
*epidermal growth factor receptor antibody: PD, pharmacology
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
fluorouracil: PD, pharmacology
folinic acid: CT, clinical trial
folinic acid: CB, drug combination
folinic acid: DT, drug therapy
folinic acid: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: CB, drug combination
gefitinib: DT, drug therapy
gefitinib: PO, oral drug administration
gefitinib: PD, pharmacology
*gelatinase B: EC, endogenous compound
gemcitabine: CT, clinical trial
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
gemcitabine: PD, pharmacology
hr 3
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide: DV, drug

development
n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide: DT, drug therapy
n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide: PD, pharmacology
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
panitumumab
pd 160678
*pyrimidine: CT, clinical trial
*pyrimidine: DV, drug development
*pyrimidine: DT, drug therapy
*pyrimidine: PD, pharmacology
*quinazoline: CT, clinical trial
*quinazoline: DV, drug development
*quinazoline: DT, drug therapy
*quinazoline: PD, pharmacology
trastuzumab
unclassified drug
RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (erlotinib) 183319-69-9, 183321-74-6; (fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gelatinase B) 146480-36-6; (gemcitabine) 103882-84-4; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide) 194423-15-9; (paclitaxel) 33069-62-4; (panitumumab) 339177-26-3; (pyrimidine) 289-95-2; (quinazoline) 253-82-7; (trastuzumab) 180288-69-1
CN (1) abx egf; (2) bibx 1382; (3) c 225; (4) ci 1033; (5) ekb 56; (6) emd 7200; (7) gw 2016; (8) hr 3; (9) iressa; (10) pd 153035; (11) pd 160678; (12) pd 168393; (13) pki 166; (14) tarceva; cetuximab; herceptin
CO (1) Abgenix; (2) Boehringer; (3) Imclone; (4) Pfizer; (5) Wyeth Ayerst; (6) Merck; (7) Glaxo; (8) york medical; (9) Astra Zeneca; (10) Parke Davis; (11) Parke Davis; (12) Parke Davis; (13) Novartis; (14) Hoffmann La Roche

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ACCESSION NUMBER:	2003416626 EMBASE Full-text
TITLE:	The impact of gefitinib on epidermal growth factor receptor signaling pathways in cancer.
AUTHOR:	Averbuch S.D.
CORPORATE SOURCE:	Dr. S.D. Averbuch, Clinical Research Oncology, AstraZeneca Pharmaceuticals LP, 1800 Concord Pike, Wilmington, DE 19850, United States. Steven.averbuch@astrazeneca.com
SOURCE:	Clinical Lung Cancer, (Sep 2003) Vol. 5, No. SUPPL. 1, pp. S5-S10. Refs: 40 ISSN: 1525-7304 CODEN: CLCLCA
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	015 Chest Diseases, Thoracic Surgery and Tuberculosis 016 Cancer 029 Clinical and Experimental Biochemistry 030 Clinical and Experimental Pharmacology 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 30 Oct 2003 Last Updated on STN: 30 Oct 2003

AB The ErbB family of receptor tyrosine kinases, of which the epidermal growth factor receptor (EGFR) is the prototype, is associated with the formation and malignant progression of most of the common solid tumors. These molecules play a key role in a complex network of signal transduction pathways that function in normal development as well as in neoplastic transformation. The EGFR and other family members are therefore promising targets for new anticancer therapies. In normal tissues, EGFR-tyrosine kinase (TK) activity is strictly controlled. However, in tumor cells, there are multiple mechanisms that can lead to increased or inappropriate EGFR-TK activity, including altered expression of EGFR, its ligand, or interacting molecules; decreased deactivation through phosphatases or downregulation; or mutation of the EGFR protein. Novel therapeutic approaches aimed at inhibiting increased EGFR-TK activity include antibodies that block the extracellular ligand-binding site, antibody or ligand fusion proteins that specifically target toxins to the tumor cells, or small-molecule TK inhibitors (TKIs) that act intracellularly to block downstream signal transduction from EGFR. Studies have shown that such blockade can lead to reduced cellular proliferation, inhibition of survival signals, and inhibition of tumor metastasis and angiogenesis. Additionally, some agents, including EGFR antibodies and TKIs such as gefitinib have been demonstrated to be effective against various human solid tumors in preclinical models and have shown activity in advanced non-small-cell lung cancer and other solid tumors.

CT Medical Descriptors:
angiogenesis
article
binding site
cancer radiotherapy
cell proliferation
cell survival
clinical trial
controlled study
disease model
down regulation
drug efficacy
drug targeting
enzyme activity
enzyme inactivation
enzyme inhibition
enzyme regulation
gene mutation
human
inhibition kinetics
ligand binding
*lung non small cell cancer: DT, drug therapy
*lung non small cell cancer: RT, radiotherapy
malignant transformation
metastasis inhibition
mouse
nonhuman
protein expression
protein family
signal transduction
solid tumor: DT, drug therapy
tumor cell
tumor xenograft

CT Drug Descriptors:
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: DV, drug development
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: DT, drug therapy
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
4 (3 chloroanilino) 6,7 dimethoxyquinazoline: DV, drug development

4 (3 chloroanilino) 6,7 dimethoxyquinazoline: DT, drug therapy
4 (3 chloroanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DV, drug development
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
ag 1515
antineoplastic agent: CT, clinical trial
antineoplastic agent: CB, drug combination
antineoplastic agent: DV, drug development
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
canertinib: DV, drug development
canertinib: DT, drug therapy
canertinib: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: DV, drug development
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
cgp 75166
*epidermal growth factor receptor: EC, endogenous compound
epidermal growth factor receptor antibody: DV, drug development
epidermal growth factor receptor antibody: DT, drug therapy
epidermal growth factor receptor antibody: PD, pharmacology
epidermal growth factor receptor kinase: EC, endogenous compound
erlotinib: CT, clinical trial
erlotinib: DV, drug development
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
*gefitinib: CT, clinical trial
*gefitinib: CB, drug combination
*gefitinib: DV, drug development
*gefitinib: DT, drug therapy
*gefitinib: PD, pharmacology
hybrid protein: EC, endogenous compound
lapatinib: DV, drug development
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
ligand: EC, endogenous compound
n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide: DV, drug development
n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide: DT, drug therapy
n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide: PD, pharmacology
pelitinib: DV, drug development
pelitinib: DT, drug therapy
pelitinib: PD, pharmacology
phosphatase: EC, endogenous compound
protein tyrosine kinase: EC, endogenous compound
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: CB, drug combination
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
receptor protein: EC, endogenous compound
su 5259
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy

unclassified drug

RN (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) 153436-53-4; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (n [4 (3 bromoanilino) 6 quinazolinyl]acrylamide) 194423-15-9; (pelitinib) 257933-82-7; (phosphatase) 9013-05-2; (protein tyrosine kinase) 80449-02-1; (trastuzumab) 180288-69-1

CN (1) ag 1478; (2) ag 1515; (3) cgp 75166; (4) ci 1033; (5) ekb 569; (6) gw 572016; (7) iressa; (8) osi 774; (9) pd 153035; (10) pd 168393; (11) pd 183805; (12) pki 166; (13) su 5259; (14) su 5271; (15) tarceva; (16) tarceva; (17) zd 1839; c 225; erbitux

CO (1) Sugen; (2) Sugen; (3) Novartis; (4) Pfizer; (5) Wyeth; (6) Glaxo SmithKline; (7) Astra Zeneca; (8) Osi; (9) Pfizer; (10) Pfizer; (11) Pfizer; (12) Novartis; (13) Sugen; (14) Sugen; (15) Genentech; (16) Osi; (17) Astra Zeneca

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ACCESSION NUMBER: 2003029475 EMBASE Full-text
TITLE: Erlotinib hydrochloride. Oncolytic EGF receptor inhibitor.
AUTHOR: Sorbera L.A.; Castaner J.; Silvestre J.S.; Bayes M.
CORPORATE SOURCE: L.A. Sorbera, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
SOURCE: Drugs of the Future, (1 Oct 2002) Vol. 27, No. 10, pp. 923-934.
Refs: 77
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2003
Last Updated on STN: 30 Jan 2003

AB The epidermal growth factor receptor (EGFR) is a type 1 receptor tyrosine kinase that is involved in the modulation of cellular differentiation and is overexpressed in many types of human cancers such as lung, pancreatic, ovarian, renal cell, gastric, hepatocellular and breast. Overexpression of EGFR is frequently correlated with increased tumor grade, increased metastatic potential and poor prognosis. Thus, inhibition of EGFR signaling is an attractive therapeutic option for the treatment of cancer. One method that can interfere with EGFR is the direct inhibition of EGFR tyrosine kinase activity. Several tyrosine kinase inhibitors have been developed and evaluated over the past 10 years of which the majority are reversible competitors with ATP for binding to the intracellular catalytic domain of the tyrosine kinase. One such EGFR tyrosine kinase inhibitor that has shown excellent antitumor activity is erlotinib hydrochloride, an oral quinazoline derivative that reversibly and selectively inhibits tyrosine kinase activity.

CT Medical Descriptors:
acne: SI, side effect
anemia: SI, side effect
*antineoplastic activity
area under the curve
cancer grading
cancer survival
carcinogenesis

cell differentiation
clinical trial
cytotoxicity
diarrhea: SI, side effect
dose response
  drug blood level
  drug clearance
  drug distribution
  drug efficacy
  drug elimination
  drug half life
  drug metabolism
  drug potentiation
  drug safety
  drug structure
  drug tissue level
  drug tolerability
enzyme activity
enzyme inhibition
epidermis hyperplasia: SI, side effect
fatigue: SI, side effect
febrile neutropenia: SI, side effect
gene overexpression
headache: SI, side effect
human
hyperbilirubinemia: SI, side effect
liver toxicity: SI, side effect
major clinical study
maximum tolerated dose
metastasis
mucosa inflammation: SI, side effect
multicenter study
nausea: SI, side effect
neutropenia: SI, side effect
peripheral neuropathy: SI, side effect
  pharmacodynamics
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
protein phosphorylation
rash: SI, side effect
review
signal transduction
skin toxicity: SI, side effect
solid tumor
steady state
stomach emptying
vomiting: CO, complication

CT Drug Descriptors:
  6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
  *canertinib: PD, pharmacology
  carboplatin: AE, adverse drug reaction
  carboplatin: CB, drug combination
  carboplatin: IT, drug interaction
  cisplatin: CB, drug combination
  cisplatin: IT, drug interaction
  docetaxel: AE, adverse drug reaction
  docetaxel: CB, drug combination
  docetaxel: IT, drug interaction

*epidermal growth factor receptor kinase
*erlotinib: CT, clinical trial
*erlotinib: AD, drug administration
*erlotinib: AN, drug analysis
*erlotinib: DV, drug development
*erlotinib: DO, drug dose
*erlotinib: IV, intravenous drug administration
*erlotinib: PO, oral drug administration
*erlotinib: PK, pharmacokinetics
*erlotinib: PD, pharmacology
*gefitinib: PD, pharmacology
genistein: PD, pharmacology
lapatinib: PD, pharmacology
neu differentiation factor
paclitaxel: AE, adverse drug reaction
paclitaxel: CB, drug combination
paclitaxel: IT, drug interaction
*pelitinib: PD, pharmacology
*protein tyrosine kinase inhibitor: PD, pharmacology
taxane derivative: CB, drug combination
taxane derivative: IT, drug interaction
unclassified drug

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carboplatin) 41575-94-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (docetaxel) 114977-28-5; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (genistein) 446-72-0; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (paclitaxel) 33069-62-4; (pelitinib) 257933-82-7

CN cp 358774; ekb 569; gw 2016; iressa; nsc 718781; osi 774; pki 166; tarceva

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ACCESSION NUMBER: 2002280437 EMBASE Full-text
TITLE: [Rational and _acques_ve treatments for lung cancer: Overview of new approaches and perspectives].
LA BIOLOGIE DES CANCERS BRONCHIQUES ET LES NOUVELLES CIBLES THERAPEUTIQUES: ETAT DES CONNAISSANCES ET PERSPECTIVES.
AUTHOR: Delord J.-P.; Caunes N.
CORPORATE SOURCE: J.-P. Delord, Institut Claudius-Regaud, Departement de Medecine, 20-24, rue du Pont-Saint-Pierre, F-31052 Toulouse Cedex, France
SOURCE: Oncologie, (2002) Vol. 4, No. 4, pp. 285-291.
Refs: 28
ISSN: 1292-3818 CODEN: OOLOFG
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 22 Aug 2002
Last Updated on STN: 22 Aug 2002

AB There have been extraordinary advances in the knowledge of oncogenesis. Selective compounds have been developed and are now considered as potential new anticancer agents targeting the mitogenic pathway, cancer progression or

neo-angiogenesis. We discuss here the therapeutic potential of these new drugs.

CT Medical Descriptors:
angiogenesis
antineoplastic activity
apoptosis
article
cancer chemotherapy
cancer growth
cancer invasion
clinical trial
drug targeting
gene expression
human
*lung cancer: DT, drug therapy

CT Drug Descriptors:
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
batimastat: DT, drug therapy
batimastat: PD, pharmacology
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
endostatin: DT, drug therapy
endostatin: PD, pharmacology
epidermal growth factor receptor
epidermal growth factor receptor antibody: CT, clinical trial
epidermal growth factor receptor antibody: DT, drug therapy
epidermal growth factor receptor antibody: PD, pharmacology
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
marimastat: DT, drug therapy
marimastat: PD, pharmacology
mdx 447: CT, clinical trial
mdx 447: DT, drug therapy
mdx 447: PD, pharmacology
monoclonal antibody: CT, clinical trial
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
monoclonal antibody h R3: CT, clinical trial
monoclonal antibody h R3: DT, drug therapy
monoclonal antibody h R3: PD, pharmacology
pelitinib: CT, clinical trial

pelitinib: DT, drug therapy
pelitinib: PD, pharmacology
prinomastat: DT, drug therapy
prinomastat: PD, pharmacology
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
rebimastat: DT, drug therapy
rebimastat: PD, pharmacology
semaxanib: CT, clinical trial
semaxanib: DT, drug therapy
semaxanib: PD, pharmacology
squalamine: CT, clinical trial
squalamine: DT, drug therapy
stem cell factor: EC, endogenous compound
tanomastat: DT, drug therapy
tanomastat: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: DT, drug therapy
thalidomide: PD, pharmacology
thrombocyte factor 4: DT, drug therapy
thrombocyte factor 4: PD, pharmacology
unclassified drug
vasculotropin antibody: CT, clinical trial
vasculotropin antibody: DT, drug therapy
vasculotropin antibody: PD, pharmacology

RN (batimastat) 130370-60-4, 130464-84-5; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (endostatin) 187888-07-9; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (marimastat) 154039-60-8; (pelitinib) 257933-82-7; (prinomastat) 192329-42-3, 195008-93-6; (rebimastat) 191537-76-5, 259188-38-0; (semaxanib) 186610-95-7; (squalamine) 148717-90-2, 160022-48-0; (tanomastat) 179545-76-7, 179545-77-8; (thalidomide) 50-35-1; (thrombocyte factor 4) 37270-94-3, 69670-74-2

CN ag 3340; bay 12 9566; bms 275291; ci 1033; ekb 569; gw 2016; imc c225; mdx 447; osi 774; pki 166; su 5416; zd 1839

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ACCESSION NUMBER: 2003048759 EMBASE Full-text
TITLE: Activation of the PI3K/Akt pathway and chemotherapeutic resistance.
AUTHOR: West K.A.; Castillo S.S.; Dennis P.A.
CORPORATE SOURCE: P.A. Dennis, Cancer Therapeutics Branch, Center for Cancer Research, National Cancer Institute, 8901 Wisconsin Avenue, Bethesda, MD 20889, United States. pdennis@nih.gov
SOURCE: Drug Resistance Updates, (Dec 2002) Vol. 5, No. 6, pp. 234-248.
Refs: 148
ISSN: 1368-7646 CODEN: DRUPFW
PUBLISHER IDENT.: S 1368-7646(02)00120-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Feb 2003
Last Updated on STN: 7 Feb 2003

AB The resistance of many types of cancer to conventional chemotherapies is a major factor undermining successful cancer treatment. In this review, the role of a signal transduction pathway comprised of the lipid kinase, phosphatidylinositol 3-kinase (PI3K), and the serine/threonine kinase, Akt (or PKB), in chemotherapeutic resistance will be explored. Activation of this pathway plays a pivotal role in essential cellular functions such as survival, proliferation, migration and differentiation that underlie the biology of human cancer. Akt activation also contributes to tumorigenesis and tumor metastasis, and as shown most recently, resistance to chemotherapy. Modulating Akt activity is now a commonly observed endpoint of chemotherapy administration or administration of chemopreventive agents. Studies performed in vitro and in vivo combining small molecule inhibitors of the PI3K/Akt pathway with standard chemotherapy have been successful in attenuating chemotherapeutic resistance. As a result, small molecules designed to specifically target Akt and other components of the pathway are now being developed for clinical use as single agents and in combination with chemotherapy to overcome therapeutic resistance. Specifically inhibiting Akt activity may be a valid approach to treat cancer and increase the efficacy of chemotherapy. Published by Elsevier Science Ltd..

CT Medical Descriptors:
*cancer: DP, drug resistance
*cancer: DT, drug therapy
cancer combination chemotherapy
*cancer resistance
carcinogenesis
cell function
cell survival
drug efficacy
enzyme activation
enzyme regulation
metastasis
priority journal
review
signal transduction

CT Drug Descriptors:
2 [[2 [[2 [(2 amino 3 mercaptopropyl)amino] 3 methylpentyl]oxy] 1 oxo 3 phenylpropyl]amino] 4 (methylsulfonyl)butanoic acid isopropyl ester: DT, drug therapy
2 [[2 [[2 [(2 amino 3 mercaptopropyl)amino] 3 methylpentyl]oxy] 1 oxo 3 phenylpropyl]amino] 4 (methylsulfonyl)butanoic acid isopropyl ester: PD, pharmacology
2 morpholino 8 phenylchromone: DT, drug therapy
2 morpholino 8 phenylchromone: PD, pharmacology
7 hydroxystaurosporine: DT, drug therapy
7 hydroxystaurosporine: PD, pharmacology
anthracycline derivative: DT, drug therapy
anthracycline derivative: PD, pharmacology
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PD, pharmacology
butyric acid: DT, drug therapy
butyric acid: PD, pharmacology
cisplatin: DT, drug therapy
cisplatin: PD, pharmacology
daunorubicin: DT, drug therapy
daunorubicin: PD, pharmacology
DNA topoisomerase inhibitor: DT, drug therapy
DNA topoisomerase inhibitor: PD, pharmacology
doxorubicin: DT, drug therapy
doxorubicin: PD, pharmacology
etoposide: DT, drug therapy

etoposide: PD, pharmacology
fr 901228: DT, drug therapy
fr 901228: PD, pharmacology
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
gemcitabine: DT, drug therapy
gemcitabine: PD, pharmacology
imatinib: DT, drug therapy
imatinib: PD, pharmacology
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
midostaurin: DT, drug therapy
midostaurin: PD, pharmacology
n [[5 [(2 amino 3 mercaptopropyl)amino][1,1' biphenyl] 2 yl]carbonyl]methionine methyl ester: DT, drug therapy
n [[5 [(2 amino 3 mercaptopropyl)amino][1,1' biphenyl] 2 yl]carbonyl]methionine methyl ester: PD, pharmacology
nucleoside analog: DT, drug therapy
nucleoside analog: PD, pharmacology
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
*phosphatidylinositol 3 kinase: EC, endogenous compound
phosphatidylinositol 3 kinase inhibitor: DT, drug therapy
phosphatidylinositol 3 kinase inhibitor: PD, pharmacology
*protein kinase B: EC, endogenous compound
staurosporine: DT, drug therapy
staurosporine: PD, pharmacology
tamoxifen: DT, drug therapy
tamoxifen: PD, pharmacology
temsirolimus: DT, drug therapy
temsirolimus: PD, pharmacology
topotecan: DT, drug therapy
topotecan: PD, pharmacology
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
unclassified drug
unindexed drug
wortmannin: DT, drug therapy
wortmannin: PD, pharmacology

RN (2 [[2 [[2 [(2 amino 3 mercaptopropyl)amino] 3 methylpentyl]oxy] 1 oxo 3 phenylpropyl]amino] 4 (methylsulfonyl)butanoic acid isopropyl ester) 160141-09-3; (2 morpholino 8 phenylchromone) 154447-36-6; (7 hydroxystaurosporine) 112953-11-4; (butyric acid) 107-92-6, 156-54-7, 461-55-2; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (doxorubicin) 23214-92-8, 25316-40-9; (etoposide) 33419-42-0; (fr 901228) 128517-07-7; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (imatinib) 152459-95-5, 220127-57-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (midostaurin) 120685-11-2; (n [[5 [(2 amino 3 mercaptopropyl)amino][1,1' biphenyl] 2 yl]carbonyl]methionine methyl ester) 170006-73-2; (paclitaxel) 33069-62-4; (phosphatidylinositol 3 kinase) 115926-52-8; (protein kinase B) 148640-14-6; (staurosporine) 62996-74-1; (tamoxifen) 10540-29-1; (temsirolimus) 162635-04-3, 343261-52-9; (topotecan) 119413-54-6, 123948-87-8; (trastuzumab) 180288-69-1; (wortmannin) 19545-26-7

CN cci 779; fr 901228; fti 277; gw 572016; l 744832; ly 294002; pkc 412; st 1571; ucn 01; zd 1839

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ACCESSION NUMBER: 2005335029 EMBASE Full-text
TITLE: Smart drugs: Tyrosine kinase inhibitors in cancer therapy.
AUTHOR: Shawver L.K.; Slamon D.; Ullrich A.
CORPORATE SOURCE: A. Ullrich, Department of Molecular Biology, Max-Planck-Institute of Biochemistry, Am Klopferspitz 18A, 82152 Martinsried, Germany. ullrich@biochem.mpg.de
SOURCE: Cancer Cell, (Mar 2002) Vol. 1, No. 2, pp. 117-123. Refs: 61
ISSN: 1535-6108 CODEN: CCAECI
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
022 Human Genetics
025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Sep 2005
Last Updated on STN: 1 Sep 2005

AB Cancer therapy directed at specific, frequently occurring molecular alterations in signaling pathways of cancer cells has been validated through the clinical development and regulatory approval of agents such as Herceptin for the treatment of advanced breast cancer and Gleevec for chronic myelogenous leukemia and gastrointestinal stromal tumors. While most novel, target-directed cancer drugs have pregenomic origins, one can anticipate a postgenomic wave of sophisticated "smart drugs" to fundamentally change the treatment of all cancers. With these prospects, interest in this new class of therapeutics extends from basic research scientists to practicing oncologists and their patients. An extension of the initial successes in molecular oncology will occur more quickly and successfully through an appreciation of lessons learned with the first group of agents in their progress through clinical development. Copyright .COPYRGT. 2002 Cell Press.

CT Medical Descriptors:
*breast carcinoma: DT, drug therapy
*cancer therapy
*chronic myeloid leukemia: DT, drug therapy
clinical trial
gene overexpression
gene targeting
genomics
human
medical practice
medical research
molecular dynamics
priority journal
review

CT Drug Descriptors:
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: DT, drug therapy

cetuximab: PD, pharmacology
epidermal growth factor receptor 2: EC, endogenous compound
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
imatinib: CT, clinical trial
imatinib: DT, drug therapy
imatinib: PD, pharmacology
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
lapatinib: PD, pharmacology
pelitinib: CT, clinical trial
pelitinib: DT, drug therapy
pelitinib: PD, pharmacology
*protein tyrosine kinase inhibitor: CT, clinical trial
*protein tyrosine kinase inhibitor: DT, drug therapy
*protein tyrosine kinase inhibitor: PD, pharmacology
semaxanib: CT, clinical trial
semaxanib: DT, drug therapy
semaxanib: PD, pharmacology
trastuzumab: CT, clinical trial
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
vandetanib: CT, clinical trial
vandetanib: DT, drug therapy
vandetanib: PD, pharmacology
vatalanib: CT, clinical trial
vatalanib: DT, drug therapy
vatalanib: PD, pharmacology

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (epidermal growth factor receptor 2) 137632-09-8; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (pelitinib) 257933-82-7; (semaxanib) 186610-95-7; (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib) 212141-54-3, 212142-18-2

CN (1) ci 1033; (2) ekb 569; (3) erbitux; (4) gleevec; (5) gw 2016; (6) herceptin; (7) iressa; (8) pki 166; (9) ptk 787; (10) ptk 787; (11) semaxanib; (12) semaxanib; (13) tarceva; (14) tarceva; (15) tarceva; (16) zd 6474

CO (1) Pfizer; (2) Wyeth; (3) Imclone; (4) Novartis; (5) Glaxo SmithKline; (6) Genentech; (7) Astra Zeneca; (8) Novartis; (9) Novartis; (10) Schering AG; (11) Pharmacia; (12) Sugen; (13) Genentech; (14) Hoffmann La Roche; (15) Osi; (16) Astra Zeneca

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ACCESSION NUMBER: 2002228993 EMBASE Full-text
TITLE: New directions in the treatment of cancer : Inhibition of signal transduction.
AUTHOR: Finley R.S.
CORPORATE SOURCE: R.S. Finley, Department of Pharmacy Practice, Philadelphia College of Pharmacy, Univ. of the Sci. in Philadelphia, 600 S 43rd St, Philadelphia, PA 19104, United States. r.finley@usip.edu
SOURCE: Journal of Pharmacy Practice, (2002) Vol. 15, No. 1, pp.

5-16.
Refs: 124
ISSN: 0897-1900 CODEN: JPPREU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jul 2002
Last Updated on STN: 18 Jul 2002

AB In recent years, it has become increasingly apparent that proteins regulated by activated oncogenes or mutated tumor suppressor genes are responsible for the transformation of normal cells to malignant cells as well as for malignant characteristics such as uncontrolled cellular proliferation and the development of metastases. These proteins may be soluble factors, receptors on cell surfaces, or intracellular enzymes that produce signals that stimulate cellular development or proliferation. This process is called signal transduction. In many cases, increased amounts of these proteins have been demonstrated in cancer cells (over normal cells) and have been found to carry prognostic significance. New approaches in cancer treatment are being designed to block such proteins; this approach is termed signal transduction inhibition. Specific protein targets that anticancer therapies have been developed to inhibit include epidermal growth factor receptors, tyrosine kinase, farnesyl transferase, and various promoters of angiogenesis.

CT Medical Descriptors:
acne: SI, side effect
article
bone marrow suppression: ET, etiology
cancer cell culture
*cancer chemotherapy
cell proliferation
cell surface
chemotherapy induced emesis: SI, side effect
clinical trial
colon carcinoma: DT, drug therapy
drug receptor binding
drug tolerability
enzyme inhibition
gene overexpression
headache: SI, side effect
human
inhibition kinetics
metastasis potential
neutropenia: DT, drug therapy
neutropenia: ET, etiology
prognosis
receptor upregulation
*signal transduction
skin defect: DT, drug therapy
skin defect: SI, side effect
*tumor suppressor gene

CT Drug Descriptors:
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: AE, adverse drug reaction
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy

3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: TO, drug toxicity
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: IV, intravenous drug administration
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: PO, oral drug administration
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: PD, pharmacology
antibiotic agent: DT, drug therapy
*antineoplastic agent: AE, adverse drug reaction
***antineoplastic agent: CT, clinical trial**
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: TO, drug toxicity
*antineoplastic agent: IV, intravenous drug administration
*antineoplastic agent: PO, oral drug administration
*antineoplastic agent: PD, pharmacology
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: PD, pharmacology
cetuximab: AE, adverse drug reaction
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: DT, drug therapy
cetuximab: TO, drug toxicity
cetuximab: PD, pharmacology
ciprofloxacin: CB, drug combination
ciprofloxacin: DT, drug therapy
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: DT, drug therapy
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: TO, drug toxicity
docetaxel: PD, pharmacology
epidermal growth factor receptor
erlotinib: AE, adverse drug reaction
erlotinib: TO, drug toxicity
erlotinib: PO, oral drug administration
erlotinib: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: CB, drug combination
gefitinib: TO, drug toxicity
gefitinib: PO, oral drug administration
gefitinib: PD, pharmacology
gemcitabine: CT, clinical trial
gemcitabine: DT, drug therapy
immunotoxin: PD, pharmacology
irinotecan: CT, clinical trial
irinotecan: CB, drug combination
irinotecan: DT, drug therapy
l 778123: CT, clinical trial
l 778123: DT, drug therapy
l 778123: PD, pharmacology
lapatinib: PD, pharmacology
lonafarnib: CT, clinical trial
lonafarnib: DT, drug therapy
lonafarnib: PD, pharmacology
mdx 447: PD, pharmacology

monoclonal antibody: PD, pharmacology
monoclonal antibody h22 egf: CT, clinical trial
monoclonal antibody h22 egf: DT, drug therapy
monoclonal antibody h22 egf: PD, pharmacology
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: PD, pharmacology
panitumumab: CT, clinical trial
panitumumab: DT, drug therapy
panitumumab: PD, pharmacology
protein farnesyltransferase
protein tyrosine kinase
protein tyrosine kinase inhibitor: PD, pharmacology
raltitrexed: CT, clinical trial
raltitrexed: CB, drug combination
raltitrexed: PD, pharmacology
retinoid: DT, drug therapy
retinoid: TP, topical drug administration
tipifarnib: AE, adverse drug reaction
tipifarnib: CT, clinical trial
tipifarnib: DT, drug therapy
tipifarnib: TO, drug toxicity
tipifarnib: PO, oral drug administration
tipifarnib: PD, pharmacology
topotecan: CT, clinical trial
topotecan: CB, drug combination
topotecan: TO, drug toxicity
topotecan: PD, pharmacology
unclassified drug
unindexed drug

RN (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (ciprofloxacin) 85721-33-1; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (irinotecan) 100286-90-6; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lonafarnib) 193275-84-2; (paclitaxel) 33069-62-4; (panitumumab) 339177-26-3; (protein tyrosine kinase) 80449-02-1; (raltitrexed) 112887-68-0; (tipifarnib) 192185-72-1; (topotecan) 119413-54-6, 123948-87-8

CN (1) imc c225; (2) mdx 447; (3) osi 774; (4) zd 1839; bms 214662; l 778123; r 115777; sch 66336

CO (1) Imclone; (2) Medarex; (3) Pfizer (United States); (4) Astra Zeneca (United States)

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ACCESSION NUMBER: 2002025346 EMBASE Full-text
TITLE: Epidermal growth factor receptor tyrosine kinase inhibitors in cancer therapy.
AUTHOR: Adjei A.A.
CORPORATE SOURCE: A.A. Adjei, Division of Medical Oncology, Mayo Clinic and Foundation, 200 First St. SW, Rochester, MN 55905, United States
SOURCE: Drugs of the Future, (2001) Vol. 26, No. 11, pp. 1087-1092. Refs: 39
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2002
Last Updated on STN: 31 Jan 2002

AB Receptor tyrosine kinases are transmembrane proteins involved in signal transduction. They propagate growth factor signals from the cell surface to intracellular processes that control critical functions such as growth, differentiation, angiogenesis and inhibition of apoptosis. In malignancies, these signaling pathways are often exploited to optimize tumor growth and metastasis. One such family of receptor tyrosine kinases is the epidermal growth factor receptor (EGFR) tyrosine kinase. These receptors are overexpressed in a wide variety of epithelial cancers and have been implicated in tumor aggressiveness. Thus, targeting the EGFR tyrosine kinase has attracted considerable attention. This review will summarize current preclinical and clinical knowledge of the small-molecule oral inhibitors of the EGFR tyrosine kinase, which include ZD-1839, OSI-774, CI-1033, EKB-569, PKI-166, GW-2016 and BIBX-1382.

CT Medical Descriptors:
antineoplastic activity
cancer research
clinical trial
diarrhea: SI, side effect
drug efficacy
drug research
drug safety
enzyme inhibition
*head and neck cancer: DT, drug therapy
human
*lung cancer: DT, drug therapy
nausea: SI, side effect
rash: SI, side effect
review
thrombocytopenia: SI, side effect
vomiting: SI, side effect

CT Drug Descriptors:
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: AE, adverse drug reaction
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: CT, clinical trial
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
*6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: DT, drug therapy
antineoplastic agent: PO, oral drug administration
antineoplastic agent: PD, pharmacology
bibx 1382: CT, clinical trial
bibx 1382: DT, drug therapy
canertinib: AE, adverse drug reaction
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PO, oral drug administration
canertinib: PD, pharmacology
epidermal growth factor receptor: EC, endogenous compound

*epidermal growth factor receptor kinase: EC, endogenous compound
*erlotinib: AE, adverse drug reaction
*erlotinib: CT, clinical trial
*erlotinib: DT, drug therapy
*erlotinib: PD, pharmacology
gefitinib: AE, adverse drug reaction
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PO, oral drug administration
gefitinib: PD, pharmacology
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
*pelitinib: AE, adverse drug reaction
*pelitinib: CT, clinical trial
*pelitinib: DT, drug therapy
*pelitinib: PD, pharmacology
*protein tyrosine kinase inhibitor: AE, adverse drug reaction
*protein tyrosine kinase inhibitor: CT, clinical trial
*protein tyrosine kinase inhibitor: DT, drug therapy
*protein tyrosine kinase inhibitor: PO, oral drug administration
*protein tyrosine kinase inhibitor: PD, pharmacology
unclassified drug

RN (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (pelitinib) 257933-82-7

CN bibx 1382; ci 1033; ekb 569; gw 2016; iressa; osi 774; pki 166; tarceva; zd 1839

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ACCESSION NUMBER: 2001261092 EMBASE Full-text
TITLE: Growth factor receptor kinase inhibitors: Recent progress and clinical impact.
AUTHOR: Dumas J.
CORPORATE SOURCE: J. Dumas, Bayer Research Center, Bayer Corporation, Pharmaceutical Division, 400 Morgan Lane, West Haven, CT 06516, United States. _acques.dumas.b@bayer.com
SOURCE: Current Opinion in Drug Discovery and Development, (2001) Vol. 4, No. 4, pp. 378-389.
Refs: 81
ISSN: 1367-6733 CODEN: CODDFF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 2001
Last Updated on STN: 16 Aug 2001

AB Inhibition of growth factor receptor kinases is one of the most promising therapeutic approaches for the treatment of cancer. This review focuses on the most recent progress in this area, and gives an overview of the compounds currently in the clinic, as well as key preclinical analogs.

CT Medical Descriptors:
cancer chemotherapy
clinical trial
drug absorption
drug activity
drug mechanism

drug research
drug structure
*enzyme inhibition
human
review
CT Drug Descriptors:
2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
4 (3 bromoanilino) 6 (methylamino)pyrido[3,4 d]pyrimidine: CT, clinical trial
4 (3 bromoanilino) 6 (methylamino)pyrido[3,4 d]pyrimidine: PD, pharmacology
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: CM, drug comparison
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine
adl 681: CT, clinical trial
adl 681: CM, drug comparison
adl 681: PK, pharmacokinetics
ag 13764: CT, clinical trial
ag 13764: PD, pharmacology
ag 13925: CT, clinical trial
ag 13925: PD, pharmacology
canertinib: CT, clinical trial
canertinib: PK, pharmacokinetics
canertinib: PD, pharmacology
cgp 59326: CT, clinical trial
cgp 59326: PK, pharmacokinetics
cgp 59326: PD, pharmacology
cgp 75166: CT, clinical trial
cgp 75166: PO, oral drug administration
cgp 75166: PK, pharmacokinetics
cgp 75166: PD, pharmacology
cl 387785: CT, clinical trial
cl 387785: PK, pharmacokinetics
cl 387785: PD, pharmacology
ct 052923
eki 785
*epidermal growth factor receptor
erlotinib: CT, clinical trial
erlotinib: CM, drug comparison
erlotinib: PK, pharmacokinetics
erlotinib: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: PK, pharmacokinetics
gefitinib: PD, pharmacology
*growth factor receptor
growth factor receptor kinase inhibitor: CT, clinical trial
growth factor receptor kinase inhibitor: PK, pharmacokinetics
growth factor receptor kinase inhibitor: PD, pharmacology
gw 2286: CT, clinical trial
gw 2286: PD, pharmacology
imatinib: CT, clinical trial
imatinib: PD, pharmacology
lapatinib
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4

quinazolinamine: CT, clinical trial
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: PK, pharmacokinetics
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: PD, pharmacology
nvp aad777: CT, clinical trial
nvp aad777: PD, pharmacology
pd 166285
pd 166866
pd 169414: CT, clinical trial
pd 169414: PD, pharmacology
PD 173074
pelitinib
*phosphotransferase inhibitor: CT, clinical trial
*phosphotransferase inhibitor: PK, pharmacokinetics
*phosphotransferase inhibitor: PD, pharmacology
*platelet derived growth factor receptor
platelet derived growth factor receptor inhibitor: CT, clinical trial
platelet derived growth factor receptor inhibitor: PK, pharmacokinetics
platelet derived growth factor receptor inhibitor: PD, pharmacology
rpr 101511: CT, clinical trial
rpr 101511: PD, pharmacology
rpr 10151a: CT, clinical trial
rpr 10151a: PO, oral drug administration
rpr 10151a: PD, pharmacology
rpr 127963
unclassified drug
unindexed drug
vandetanib: CT, clinical trial
vandetanib: PD, pharmacology
*vasculotropin inhibitor: CT, clinical trial
*vasculotropin inhibitor: PK, pharmacokinetics
*vasculotropin inhibitor: PD, pharmacology
vatalanib: CT, clinical trial
vatalanib: PD, pharmacology
wo 09917769

RN (2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine) 179343-17-0; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (4 (3 bromoanilino) 6 (methylamino)pyrido[3,4 d]pyrimidine) 171179-06-9; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gw 2286) 601517-74-2; (imatinib) 152459-95-5, 220127-57-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine) 257938-36-6; (pelitinib) 257933-82-7; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib) 212141-54-3, 212142-18-2

CN (1) ag 13764; (2) ag 13925; (3) cgp 59326; (4) ci 1033; (5) ct 052923; (6) ekb 569; (7) eki 785; (8) gw 2016; (9) gw 2286; (10) nvp aad777; (11) osi 774; (12) pd 089828; (13) pd 153035; (14) pd 158780; (15) pd 166285; (16) pd 166866; (17) pd 169414; (18) pd 173074; (19) pki 166; (20) ptk 787; (21) rpr 101511; (22) rpr 127963; (23) sti 571; (24) su 5416; (25) su 6668; (26) wo 09917769; (27) zd 1839; (28) zd 4190; (29) zd 6474

CO (1) Pfizer; (2) Pfizer; (3) Novartis; (4) Pfizer; (5) Cor Therapeutics; (6) Wyeth Ayerst; (7) Wyeth Ayerst; (8) Glaxo SmithKline; (9) Glaxo SmithKline; (10) Novartis; (11) Pfizer; (12) Pfizer; (13) Zeneca; (14) Pfizer; (15) Pfizer; (16) Pfizer; (17) Pfizer; (18) Pfizer; (19) Novartis; (20) Novartis; (21) Aventis; (22) Aventis; (23)

Novartis; (24) Sugen; (25) Sugen; (26) BASF; (27) Astra Zeneca; (28) Astra Zeneca; (29) Astra Zeneca

***** INVENTOR RESULTS *****

```
=> d his l35

     (FILE 'HCAPLUS' ENTERED AT 10:25:57 ON 28 JAN 2008)
L35             1 S ((L8) AND (L32 OR L33 OR L34)) OR (L8 AND L1)

=> d que l35
L1              1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  US20070208023/PN
L3              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "BENZENESULFONAMIDE,
                  5-((4-((1,2-DIMETHYL-1H-BENZIMIDAZOL-5-YL)METHYLAMINO)-2-PYRIMI
                  DINYL)AMINO)-2-METHYL-"/CN
L5              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "4-QUINAZOLINAMINE, N-(3-CHLO
                  RO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL
                  )ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L6              1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3
L7            253 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L8              1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND L7
L32          5805 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KUMAR R?/AU
L33            60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MULLIN R?/AU
L34            83 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GILMER T?/AU
L35             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L8) AND (L32 OR L33 OR
                  L34)) OR (L8 AND L1)


=> d his l55

     (FILE 'MEDLINE, BIOSIS, DRUGU, BIOTECHNO, EMBASE' ENTERED AT 10:28:55 ON
     28 JAN 2008)
L55            17 S L53 NOT L54

=> d que l55
L5              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "4-QUINAZOLINAMINE, N-(3-CHLO
                  RO-4-((3-FLUOROPHENYL)METHOXY)PHENYL)-6-(5-(((2-(METHYLSULFONYL
                  )ETHYL)AMINO)METHYL)-2-FURANYL)-"/CN
L15        574067 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (CODRUG# OR COADMIN? OR
                  CONCOMITANT? OR CONCURRENT? OR BLEND? OR MIXTURE?)/OBI
L19        827880 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CANCER# OR NEOPLASM? OR
                  CARCINOMA OR TUMOR# OR TUMOUR#
L32          5805 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KUMAR R?/AU
L33            60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MULLIN R?/AU
L34            83 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GILMER T?/AU
L37          1013 SEA L5
L39      13128318 SEA (DRUG# OR PRODRUG# OR PHARMA? OR CHEMOTHERAP?)
L42        216675 SEA (TREAT# OR TREATMENT# OR TREATING# OR PREVENT? OR INHIB?)
                  (2W) (CANCER# OR NEOPLASM? OR TUMOR# OR TUMOUR#)
L43           184 SEA L37 AND L42
L44           182 SEA L43 AND L39
L45            27 SEA L44 AND (AY<2004 OR PY<2004 OR PRY<2004)
L46          1001 SEA L37 AND (L15 OR (COMBINAT? (W) CHEMOTHERAP? OR THERAP? OR
                  TREATMENT# OR PHARMAC?))
L47           102 SEA L46 AND (AY<2004 OR PY<2004 OR PRY<2004)
L49            16 SEA L32 AND (L33 OR L34)
L50            30 SEA L33 AND L34
L51            43 SEA (L49 OR L50) AND L19
L52            28 SEA L47 AND L42
L53            18 SEA L51 AND L42
L54            28 SEA L52 OR L45
L55            17 SEA L53 NOT L54
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=> dup rem l35 l55
FILE 'HCAPLUS' ENTERED AT 10:54:52 ON 28 JAN 2008
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 10:54:52 ON 28 JAN 2008

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PROCESSING COMPLETED FOR L35
PROCESSING COMPLETED FOR L55
L58           10 DUP REM L35 L55 (8 DUPLICATES REMOVED)
                 ANSWER '1' FROM FILE HCAPLUS
                 ANSWERS '2-5' FROM FILE MEDLINE
                 ANSWERS '6-7' FROM FILE BIOSIS
                 ANSWERS '8-10' FROM FILE DRUGU

=> d l58 ibib ab 1-10

L58  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2005:1196402  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:452849
TITLE:                    Pyrimidine derivatives and quinazoline derivatives for
                          cancer treatment
INVENTOR(S):              Mullin, Robert John; Gilmer, Tona M.
PATENT ASSIGNEE(S):       Smithkline Beecham Corporation, USA; Kumar, Rakesh
SOURCE:                   PCT Int. Appl., 75 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------------    ----   --------    --------------------   --------
     WO 2005105094        A2    20051110    WO 2005-US12337        20050412
     WO 2005105094        A3    20060615
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
             SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
             ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     EP 1755394           A2    20070228    EP 2005-735666         20050412
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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JP 2007532658	T	20071115	JP 2007-508465		20050412
US 2007208023	A1	20070906	US 2006-599967		20061016 <--
PRIORITY APPLN. INFO.:			US 2004-563285P	P	20040416
			US 2004-605288P	P	20040827
			WO 2005-US12337	W	20050412

OTHER SOURCE(S): MARPAT 143:452849

AB A method for treating cancer is described including administration of a pyrimidine derivative and a quinazoline derivative Also described is a pharmaceutical composition including the same. Compound preparation is included.

L58 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2007402650 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 17620431

TITLE: Pharmacokinetic-pharmacodynamic correlation from mouse to human with pazopanib, a multikinase angiogenesis inhibitor with potent antitumor and antiangiogenic activity.

AUTHOR: Kumar Rakesh; Knick Victoria B; Rudolph Sharon K; Johnson Jennifer H; Crosby Renae M; Crouthamel Ming-Chih; Hopper Teresa M; Miller Charles G; Harrington Laura E; Onori James A; Mullin Robert J; Gilmer Tona M; Truesdale Anne T; Epperly Andrea H; Boloor Amogh; Stafford Jeffrey A; Luttrell Deirdre K; Cheung Mui

CORPORATE SOURCE: Oncology Biology, GlaxoSmithKline, 1250 South Collegeville Road, UP1450, Collegeville, PA 19426, USA.. rakesh.2.kumar@gsk.com

SOURCE: Molecular cancer therapeutics, (2007 Jul) Vol. 6, No. 7, pp. 2012-21. Journal code: 101132535. ISSN: 1535-7163.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200709

ENTRY DATE: Entered STN: 11 Jul 2007
Last Updated on STN: 20 Sep 2007
Entered Medline: 19 Sep 2007

AB With the development of targeted therapeutics, especially for small-molecule inhibitors, it is important to understand whether the observed in vivo efficacy correlates with the modulation of desired/intended target in vivo. We have developed a small-molecule inhibitor of all three vascular endothelial growth factor (VEGF) receptors (VEGFR), platelet-derived growth factor receptor, and c-Kit tyrosine kinases, pazopanib (GW786034), which selectively inhibits VEGF-induced endothelial cell proliferation. It has good oral exposure and inhibits angiogenesis and tumor growth in mice. Because bolus administration of the compound results in large differences in C(max) and C(trough), we investigated the effect of continuous infusion of a VEGFR inhibitor on tumor growth and angiogenesis. GW771806, which has similar enzyme and cellular profiles to GW786034, was used for these studies due to higher solubility requirements for infusion studies. Comparing the pharmacokinetics by two different routes of administration (bolus p.o. dosing and continuous infusion), we showed that the antitumor and antiangiogenic activity of VEGFR inhibitors is dependent on steady-state concentration of the compound above a threshold. The steady-state concentration required for these effects is consistent with the concentration required for the inhibition of VEGF-induced VEGFR2 phosphorylation in mouse lungs. Furthermore, the steady-state concentration of pazopanib determined from preclinical activity showed a strong correlation with the pharmacodynamic effects and antitumor activity in the phase I clinical trial.

L58 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004485689 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15328520
TITLE: Antitumour efficacy of VEGFR2 tyrosine kinase inhibitor correlates with expression of VEGF and its receptor VEGFR2 in tumour models.
AUTHOR: Dev I K; Dornsife R E; Hopper T M; Onori J A; Miller C G; Harrington L E; Dold K M; Mullin R J; Johnson J H; Crosby R M; Truesdale A T; Epperly A H; Hinkle K W; Cheung M; Stafford J A; Luttrell D K; Kumar R
CORPORATE SOURCE: GlaxoSmithKline, Five Moore Drive, Research Triangle Park, NC 27709, USA.
SOURCE: British journal of cancer, (2004 Oct 4) Vol. 91, No. 7, pp. 1391-8.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 30 Sep 2004
Last Updated on STN: 3 Nov 2004
Entered Medline: 2 Nov 2004

AB During the development of indazolylpyrimidines as novel and potent inhibitors of vascular endothelial growth factor (VEGF) receptor-2 (VEGFR2) tyrosine kinase, we observed that some human tumour xenografts are more sensitive to VEGFR2 kinase inhibitors than others. A better understanding of the basis for this differential response may help to identify a predictive marker that would greatly aid in the identification of a suitable patient population for treatment. One representative compound from the indazolylpyrimidine series is GW654652 that inhibited all three VEGFRs with similar potency. The inhibition of VEGFR2 kinase by GW654652 was about 150 to >8800 more potent than the inhibition of eight other kinases tested. GW654652 inhibited VEGF- and bFGF-induced proliferation in endothelial cells with an IC(50) of 110 and 1980 nM, respectively, and has good pharmacokinetic profile in mouse and dog. We investigated the association between VEGF and VEGFR2 expression and the antitumour efficacy of GW654652, in various xenograft models. Statistically significant associations were observed between the antitumour efficacy of GW654652 in xenografts and VEGF protein (P=0.005) and VEGFR2 expression (P=0.041). The oral dose of GW654652 producing 50% inhibition of tumour growth (ED(50)) decreased with increasing levels of VEGF (r=-0.94); and, in contrast, the ED(50) increased with the increased expression of VEGFR2 (r=0.82). These results are consistent with the observed inverse correlation between VEGF and VEGFR2 expression in tumours. These findings support the hypothesis that VEGF and VEGFR2 expression by tumours may predict the therapeutic outcome of VEGFR kinase inhibitors.

L58 ANSWER 4 OF 10 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003125353 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12639547
TITLE: Discovery and biological evaluation of potent dual ErbB-2/EGFR tyrosine kinase inhibitors: 6-thiazolylquinazolines.
AUTHOR: Gaul Micheal D; Guo Yu; Affleck Karen; Cockerill G Stuart; Gilmer Tona M; Griffin Robert J; Guntrip Stephen; Keith Barry R; Knight Wilson B; Mullin Robert J; Murray Doris M; Rusnak David W; Smith Kathryn; Tadepalli

Sarva; Wood Edgar R; Lackey Karen
CORPORATE SOURCE: GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, NC 27709, USA.
SOURCE: Bioorganic & medicinal chemistry letters, (2003 Feb 24) Vol. 13, No. 4, pp. 637-40. Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 18 Mar 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 20 Nov 2003

AB We have identified a novel class of 6-thiazolylquinazolines as potent and selective inhibitors of both ErbB-2 and EGFR tyrosine kinase activity, with IC(50) values in the nanomolar range. These compounds inhibited the growth of both EGFR (HN5) and ErbB-2 (BT474) over-expressing human tumor cell lines in vitro. Using xenograft models of the same cell lines, we found that the compounds given orally inhibited in vivo tumor growth significantly compared with control animals.

L58 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002705778 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12467226
TITLE: The effects of the novel, reversible epidermal growth factor receptor/ErbB-2 tyrosine kinase inhibitor, GW2016, on the growth of human normal and tumor-derived cell lines in vitro and in vivo.
AUTHOR: Rusnak D W; Lackey K; Affleck K; Wood E R; Alligood K J; Rhodes N; Keith B R; Murray D M; Knight W B; Mullin R J; Gilmer T M
CORPORATE SOURCE: Department of Cancer Biology, GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, NC 27709, USA.
SOURCE: Molecular cancer therapeutics, (2001 Dec) Vol. 1, No. 2, pp. 85-94. Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 17 Dec 2002
Last Updated on STN: 28 Jan 2003
Entered Medline: 27 Jan 2003

AB The epidermal growth factor receptor (EGFR) and ErbB-2 transmembrane tyrosine kinases are currently being targeted by various mechanisms in the treatment of cancer. GW2016 is a potent inhibitor of the ErbB-2 and EGFR tyrosine kinase domains with IC50 values against purified EGFR and ErbB-2 of 10.2 and 9.8 nM, respectively. This report describes the efficacy in cell growth assays of GW2016 on human tumor cell lines overexpressing either EGFR or ErbB-2: HN5 (head and neck), A-431 (vulva), BT474 (breast), CaLu-3 (lung), and N87 (gastric). Normal human foreskin fibroblasts, nontumorigenic epithelial cells (HB4a), and nonoverexpressing tumor cells (MCF-7 and T47D) were tested as negative controls. After 3 days of compound exposure, average IC50 values for growth inhibition in the EGFR- and ErbB-2-overexpressing tumor cell lines were < 0.16 microM. The average selectivity for the tumor cells versus the human foreskin fibroblast cell line was 100-fold. Inhibition of EGFR and ErbB-2

receptor autophosphorylation and phosphorylation of the downstream modulator, AKT, was verified by Western blot analysis in the BT474 and HN5 cell lines. As a measure of cytotoxicity versus growth arrest, the HN5 and BT474 cells were assessed in an outgrowth assay after a transient exposure to GW2016. The cells were treated for 3 days in five concentrations of GW2016, and cell growth was monitored for an additional 12 days after removal of the compound. In each of these tumor cell lines, concentrations of GW2016 were reached where outgrowth did not occur. Furthermore, growth arrest and cell death were observed in parallel experiments, as determined by bromodeoxyuridine incorporation and propidium iodide staining. GW2016 treatment inhibited tumor xenograft growth of the HN5 and BT474 cells in a dose-responsive manner at 30 and 100 mg/kg orally, twice daily, with complete inhibition of tumor growth at the higher dose. Together, these results indicate that GW2016 achieves excellent potency on tumor cells with selectivity for tumor versus normal cells and suggest that GW2016 has value as a therapy for patients with tumors overexpressing either EGFR or ErbB-2.

L58 ANSWER 6 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:510480 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100510480
TITLE: GW2016, a dual inhibitor of ErbB-2 and EGFR tyrosine kinases: Effects on receptor tyrosine autophosphorylation, downstream signaling intermediaries, and in vivo anti-tumor activity.
AUTHOR(S): Xia, Wenle [Reprint author]; Mullin, Robert [Reprint author]; Keith, Barry [Reprint author]; Rusnak, David [Reprint author]; Alligood, Krystal [Reprint author]; Owens, Gary [Reprint author]; Murray, Doris [Reprint author]; Crosby, Renae [Reprint author]; Finlay, Cathy [Reprint author]; Gilmer, Tona [Reprint author]; Lackey, Karen [Reprint author]; Knight, Blaine [Reprint author]; Lucas, Sol [Reprint author]; Spector, Neil [Reprint author]
CORPORATE SOURCE: GlaxoWellcome Inc., Research Triangle Park, NC, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 675. print. Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001. ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001 Last Updated on STN: 23 Feb 2002

L58 ANSWER 7 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:216581 BIOSIS Full-text
DOCUMENT NUMBER: PREV199900216581
TITLE: Drug discovery efforts toward the identification of cRaf1 kinase inhibitors as anti-cancer agents.
AUTHOR(S): Lackey, K.; Chapman, D.; Crosby, R. M.; Davenport, E.; Dickerson, S.; Gilmer, T. M.; Griffin, R. J.; Hunter, R. N.; Jung, D. K.; Keith, B. R.; Mahoney, W. B.; McDonald, O. B.; Mullin, R. J.; Rusnak, D. W.; Wood, E.
CORPORATE SOURCE: Glaxo Wellcome Inc., 5 Moore Drive, Research Triangle Park, NC 27709, USA

SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 124. print. Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research. Philadelphia, Pennsylvania, USA. April 10-14, 1999. American Association for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999

L58 ANSWER 8 OF 10 DRUGU COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-10695 DRUGU P Full-text
TITLE: Inhibition of VEGFR2 phosphorylation correlates with anti-tumor and anti-angiogenic activity of VEGFR inhibitors in mice.
AUTHOR: Kumar R; Harrington L E; Hopper T M; Miller C G; Onori J A; Cheung M; Stafford J A; Epperly A H; Gilmer T M
CORPORATE SOURCE: GlaxoSmithKline
LOCATION: Res Triangle Pk, NC, USA
SOURCE: Clin.Cancer Res. (11, No. 24, Pt. 2, 9032S-3S, 2005) 0 Ref.
CODEN: CCREF ISSN: 1078-0432
AVAIL. OF DOC.: GlaxoSmithKline, Res Triangle Pk, NC, USA.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB With the development of targeted therapeutics, especially for small molecule inhibitors, it is important to understand whether the observed in-vivo efficacy correlates with the modulation of desired/intended target in-vivo. Previously, the Authors developed a small molecule inhibitor of all 3 VEGF receptor (VEGFR) tyrosine kinases, GW-786034. Here, they report on the pharmacokinetics (PK) and pharmacodynamics of a related compound, GW-771806, administered as a continuous infusion or bolus p.o. dose, in mice. It was confirmed that inhibition of VEGFR2 phosphorylation correlated with antitumor and antiangiogenic activity of this VEGFR inhibitor. (conference abstract: International Conference on Molecular Targets and Cancer Therapeutics, Philadelphia, U.S.A., 14/11/2005-18/11/2005).

L58 ANSWER 9 OF 10 DRUGU COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-04184 DRUGU P Full-text
TITLE: Antitumor activity of GW2016 in the EGFR positive human head and neck cancer xenograft, HN5.
AUTHOR: Mullin R J; Alligood K J; Allen P P; Crosby R M; Keith B R; Lackey K; Gilmer T M; Griffin R J; Murray D M; Tadepalli S M
CORPORATE SOURCE: GlaxoWellcome
LOCATION: Research Triangle Park, N.C., USA
SOURCE: Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 854, 2001) ISSN: 0197-016X
AVAIL. OF DOC.: Glaxo Wellcome R&D, Research Triangle Park, NC, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB GW-2016 inhibited tumor growth in animals bearing epidermal growth factor receptor (EGFR) positive head and neck cancer HN5 xenografts. In a parallel pharmacokinetics study, steady-state plasma concentrations of GW-2016 were dose-proportional and correlated with anti-tumor response. The general appearance of study animals and their normal clinical chemistry suggested that GW-2016 was not toxic at 30 and 100 mg/kg b.i.d. Treatment with GW-2016 reduced tumor EGFR phosphotyrosine (p-Tyr) levels. The Authors' results show that GW-2016 strongly inhibits HN5 growth, and suggest its mechanism of action is based upon inhibition of EGFR tyrosine kinase activity. (conference abstract: 92nd Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, USA, 2001).

L58 ANSWER 10 OF 10 DRUGU COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-04072 DRUGU P Full-text
TITLE: Anti-tumor activity of GW2016 in the ErbB-2 positive human breast cancer xenograft, BT474.
AUTHOR: Keith B R; Allen P P; Alligood K J; Crosby R M; Lackey K; Gilmer T M; Mullin R J
CORPORATE SOURCE: GlaxoWellcome
LOCATION: Research Triangle Park, N.C., USA
SOURCE: Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 803, 2001) ISSN: 0197-016X
AVAIL. OF DOC.: Glaxo Wellcome, Research Triangle Park, N.C., U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB GW-2016 exhibited antitumor activity in animals with ErbB-2 positive human ductal breast carcinoma (BT474) xenografts. GW-2016 is a selective dual inhibitor of ErbB-2 and EGF-receptor protein tyrosine kinases. (conference abstract: 92nd Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, USA, 2001).

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L3             1 SEA ABB=ON  PLU=ON  "BENZENESULFONAMIDE, 5-((4-((1,2-DIMETHYL-1
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L10         28 SEA ABB=ON  PLU=ON  L7 AND (AY<2004 OR PY<2004 OR PRY<2004)
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               E E3+ALL
L11     538951 SEA ABB=ON  PLU=ON  NEOPLASM+OLD,NT/CT
               E CARCINOMA/CT
               E E3+ALL
               E E3+OLD/CT
L12      94573 SEA ABB=ON  PLU=ON  CARCINOMA/CT
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               E E3+ALL
L13      27398 SEA ABB=ON  PLU=ON  "COMBINATION CHEMOTHERAPY"+UF/CT
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L16       4809 SEA ABB=ON  PLU=ON  DRUG DELIVERY SYSTEMS+OLD/CT (L) COMB?
L17      43372 SEA ABB=ON  PLU=ON  DRUG INTERACTIONS+OLD,NT/CT
               E ANTITUMOR AGENTS/CT
               E E3+ALL
L18     258414 SEA ABB=ON  PLU=ON  "ANTITUMOR AGENTS"+OLD,UF/CT
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L20     538951 SEA ABB=ON  PLU=ON  L11 OR L12
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L25          9 SEA ABB=ON  PLU=ON  L24 AND (AY<2004 OR PY<2004 OR PRY<2004)
L26         19 SEA ABB=ON  PLU=ON  L10 NOT L25
L27        244 SEA ABB=ON  PLU=ON  L7 AND (L18 OR L19 OR L20)
L28         24 SEA ABB=ON  PLU=ON  L27 AND (AY<2004 OR PY<2004 OR PRY<2004)
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     FILE 'REGISTRY' ENTERED AT 10:21:16 ON 28 JAN 2008
L31          1 SEA ABB=ON  PLU=ON  231277-92-2/RN
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L33         60 SEA ABB=ON  PLU=ON  MULLIN R?/AU
L34         83 SEA ABB=ON  PLU=ON  GILMER T?/AU
L35          1 SEA ABB=ON  PLU=ON  ((L8) AND (L32 OR L33 OR L34)) OR (L8 AND
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     28 JAN 2008
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L37        1013 SEA ABB=ON  PLU=ON  L5
                D COST
L38         982 SEA ABB=ON  PLU=ON  L37 AND L19
L39    13128318 SEA ABB=ON  PLU=ON  (DRUG# OR PRODRUG# OR PHARMA? OR CHEMOTHERA
                P?)
L40         966 SEA ABB=ON  PLU=ON  L38 AND L39
L41          10 SEA ABB=ON  PLU=ON  DRUG DELIVERY SYSTEM# AND L40
                D SCAN
                D TI KWIC 1-5
L42      216675 SEA ABB=ON  PLU=ON  (TREAT# OR TREATMENT# OR TREATING# OR
                PREVENT? OR INHIB?) (2W) (CANCER# OR NEOPLASM? OR TUMOR# OR
                TUMOUR#)
L43         184 SEA ABB=ON  PLU=ON  L37 AND L42
L44         182 SEA ABB=ON  PLU=ON  L43 AND L39
L45          27 SEA ABB=ON  PLU=ON  L44 AND (AY<2004 OR PY<2004 OR PRY<2004)
L46        1001 SEA ABB=ON  PLU=ON  L37 AND (L15 OR (COMBINAT? (W) CHEMOTHERAP?
                 OR THERAP? OR TREATMENT# OR PHARMAC?))
L47         102 SEA ABB=ON  PLU=ON  L46 AND (AY<2004 OR PY<2004 OR PRY<2004)
L48          97 SEA ABB=ON  PLU=ON  L47 AND L19
                SAVE TEMP L45 PAG967MULTI/A
L49          16 SEA ABB=ON  PLU=ON  L32 AND (L33 OR L34)
L50          30 SEA ABB=ON  PLU=ON  L33 AND L34
L51          43 SEA ABB=ON  PLU=ON  (L49 OR L50) AND L19
L52          28 SEA ABB=ON  PLU=ON  L47 AND L42
L53          18 SEA ABB=ON  PLU=ON  L51 AND L42
L54          28 SEA ABB=ON  PLU=ON  L52 OR L45
                SAVE TEMP L54 PAG967MULTI/A
L55          17 SEA ABB=ON  PLU=ON  L53 NOT L54
                SAVE TEMP L55 PAG967MULTIN/A

     FILE 'STNGUIDE' ENTERED AT 10:47:17 ON 28 JAN 2008

     FILE 'REGISTRY' ENTERED AT 10:48:05 ON 28 JAN 2008
                D IDE L3

     FILE 'STNGUIDE' ENTERED AT 10:48:17 ON 28 JAN 2008
                D QUE L6

     FILE 'HCAPLUS' ENTERED AT 10:48:37 ON 28 JAN 2008
                D L6 IBIB AB

     FILE 'STNGUIDE' ENTERED AT 10:48:37 ON 28 JAN 2008

     FILE 'REGISTRY' ENTERED AT 10:48:58 ON 28 JAN 2008
                D L5 IDE

     FILE 'STNGUIDE' ENTERED AT 10:49:08 ON 28 JAN 2008
                D QUE L7

     FILE 'HCAPLUS' ENTERED AT 10:50:55 ON 28 JAN 2008
L56           0 SEA ABB=ON  PLU=ON  L30 NOT L10
                D QUE L10
                D QUE L8
                D L8 IBIB AB
                D QUE L30
                D QUE L54

     FILE 'HCAPLUS, BIOSIS, EMBASE' ENTERED AT 10:52:51 ON 28 JAN 2008
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L57          51 DUP REM L30 L54 (1 DUPLICATE REMOVED)
                    ANSWERS '1-24' FROM FILE HCAPLUS
                    ANSWER '25' FROM FILE BIOSIS
                    ANSWERS '26-51' FROM FILE EMBASE
               D L57 1-24 IBIB ED ABS HITSTR HITIND
               D L57 25-51 IBIB AB HITIND
               D QUE L35
               D QUE L55

     FILE 'HCAPLUS, MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 10:54:52 ON 28
     JAN 2008
L58          10 DUP REM L35 L55 (8 DUPLICATES REMOVED)
                    ANSWER '1' FROM FILE HCAPLUS
                    ANSWERS '2-5' FROM FILE MEDLINE
                    ANSWERS '6-7' FROM FILE BIOSIS
                    ANSWERS '8-10' FROM FILE DRUGU
               D L58 IBIB AB 1-10
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